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Kinome expression profiling to target new therapeutic avenues in multiple myeloma

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Abstract

Multiple myeloma account for approximately 10% of hematological malignancies and is the second most common hematological disorder. Kinases inhibitors are widely used and demonstrated their efficiency for the treatment of cancers. Here, in order to identify kinases with potential therapeutic interest in multiple myeloma, we investigated the prognostic impact of the kinome expression profile in large cohorts of patients. We identified 36 kinome-related genes significantly linked with a prognostic value in multiple myeloma, and built a Kinome index based on their expression. Kinome index is linked to prognosis, proliferation, differentiation, and relapse in multiple myeloma. We then tested inhibitors targeting seven of the identified protein kinases (PBK, SRPK1, CDC7-DBF4, MELK, CHK1, PLK4, MPS1/TTK) in human myeloma cell lines. All tested inhibitors significantly reduced viability of myeloma cell lines, and we confirmed the potential clinical interest of three of them on primary myeloma cells from patients. In addition, we demonstrated their ability to potentialize the toxicity of conventional treatments, including Melphalan and Lenalidomide. This highlights their potential benefic effect in myeloma therapy. Three kinases inhibitors (CHK1i, MELKi and PBKi) overcome resistance to Lenalidomide, while CHK1, PBK and DBF4 inhibitors re-sensitized Melphalan resistant cell line to this conventional therapeutic agent. Altogether, we demonstrate that kinase inhibitors could be of therapeutic interest especially in high-risk myeloma patients defined by the Kinome Index. CHEK1, MELK, PLK4, SRPK1, CDC7-DBF4, MPS1/TTK and PBK inhibitors could represent new treatment options alone or in combination with Melphalan or IMiDs for refractory/relapsing myeloma patients.

Introduction

Multiple Myeloma (MM) is the second most common hematological disorder[1], and is characterized by the clonal accumulation of malignant plasma cells in the bone marrow[2]. MM is a genetically and clinically heterogeneous disease and genome sequencing studies have recently revealed considerable heterogeneity and genomic instability, a complex mutational landscape and a branching pattern of clonal evolution[3,4].

Novel agents have been developed in MM including the proteasome inhibitors bortezomib and carfilzomib, and the immunomodulatory drugs thalidomide, Lenalidomide and pomalidomide[5]. However, patients invariably relapse after multiple lines of treatment, with shortened intervals in between relapses, and finally become resistant to any treatment, resulting in loss of clinical control over the disease. It thus remains an unmet need for new therapeutic approaches to improve treatment of MM patients.

Protein kinases are key actors in various cancers where they are involved in proliferation, survival, migration but also drug resistance[6]. Protein kinases have been a potent source of targets for cancer treatment with inhibitors already approved or in clinical evaluation in numbers of malignancies. Kinases represent interesting druggable targets in MM. Indeed, whereas major signaling pathways have been studied in myeloma, they only represent a small proportion of the whole kinome[7].

In a first study, Tiedemann and colleagues[8] used a high-throughput systematic RNA interference approach to investigate kinome in Human Myeloma Cell Lines (HMCLs) and identified potential new targets for MM therapy. Here, we investigated the kinome expression profiling in large cohorts of MM patients to identify key targets and new synergistic combinations with conventional treatment. We used a list of kinases

or kinase-related genes[9] and investigated the prognostic impact of the kinome expression profile in MM. We identified 36 kinases significantly involved in patient's outcome in three independent cohorts and analyzed further the potential impact of selected available kinases inhibitors in HMCLs and primary human myeloma cells. We thus provide a list of protein kinases representing potent therapeutic targets for high-risk MM patients and propose new synergistic combinations of kinase inhibitors and conventional MM treatment.

Methods

Gene expression profiling and statistical analyses

We used the gene expression profiling (GEP) from three independent cohorts constituted of MM cells (MMCs) purified from untreated patients: the Heidelberg–Montpellier of 206 patients (ArrayExpress public database under accession number E-MTAB-362)[10,11] the UAMS-TT2 cohort of 345 patients from the University of Arkansas for Medical Sciences (UAMS, Little Rock, AR, USA; accession number GSE2658)[12], and the UAMS-TT3 cohort of 158 patients (E-TABM-1138, accession number GSE4583)[13]. Gene expression data were normalized with the MAS5 algorithm and processing of the data was performed using the webtool genomicscape (http://www.genomicscape.com)[14]. STRING webtool (https://string-db.org) was used to evaluate interconnections between genes and analyzed the enriched pathways. Cluster (v2.11) and Tree View were used to visualize gene expression data[15]. Univariate and multivariate analysis of genes prognostic for patients' survival was performed using the Cox proportional hazard model.

Multiple myeloma cell lines.

Human Myeloma Cell lines (HMCL) AMO-1 and OPM2 were purchased from DSMZ (Braunschweig, Germany), XG1 and XG21 were obtained as described[16]. HMCLs were cultured in RPMI 1640 medium, 10% FCS (control medium). For XG - IL-6 dependent HMCLs 2□ng/ml IL-6 was added. Cells were cultured in 96-well flat-bottom microtiter plates in the presence of a concentration range of selected compounds: AZD7762/CHK1i and OTSSP167/MELKi (Selleck, euromedex), HITOPK032/PBKi, XL413/CDC7-DBF4i, SRPIN340/SRPK1i (Sigma), AZ3146/MPS1i, Centrinone B/PLK4i (Tocris). Cell Titer Glo Luminescent Assay (Promega, Madison, WI, USA) was used to assess cell viability, and the 50% inhibition (IC50) was determined using GraphPad Prism software (http://www.graphpad.com/scientific-software/prism/).

The 5T33vv cells originated spontaneously in aging C57BL/KaLwRij mice and have since been propagated in vivo by intravenous transfer of the diseased marrow in young syngeneic mice[17].

Primary multiple myeloma cells

Bone marrow of patients presenting with previously untreated MM (*N*=5) at the university hospital of Montpellier was obtained after patients' written informed consent in accordance with the Declaration of Helsinki and agreement of IRB and the Montpellier University Hospital Centre for Biological Resources (DC-2008-417). Primary myeloma cells of patients were cultured with or without graded concentrations of selected inhibitors and MMC cytotoxicity evaluated using anti-CD138-Phycoerythrin monoclonal antibody (clone B-A38) and CD38-Allophycocyanin (clone-LS198-4-3) (Beckman-Coulter) as described[11]. In each culture group, viability (trypan blue) and cell counts were assayed and the percentage of $CD138^+$ viable myeloma cells was determined by flow cytometry.

Supplementary information concerning methodology are included in Supplementary experiment procedures.

Results

Identification of 36 kinome-related targets linked to prognosis in three independent multiple myeloma (MM) cohorts.

Considering the crucial role played by protein kinases in pathologies, including Multiple Myeloma (MM), we first aimed to identify kinome-related genes associated with prognostic value in MM. A list of 661 genes extracted from literature, representing 661 kinases or kinase-related genes[9] (Supplementary Table S1) were thus tested for their prognostic value in the Heidelberg-Montpellier cohort (N=206) using Maxstat algorithm[10,11]. Among the 661 genes investigated, the expression of 104 demonstrated a significant prognostic value after Benjamini Hochberg multiple testing correction. We searched to validate the prognostic value of the 104 selected kinases in two other independent cohorts of newly diagnosed patients (UAMS-TT2[12] and UAMS-TT3[13]) and defined a final list of 36 kinases with significant prognostic value in the three cohorts (Figure 1A and Supplementary Table S2). Among the 36 kinase or kinase-related genes identified, 8 of them were associated with a favorable prognosis (*AZU1; CDKN1A; DDR1; HK3; MAP4K2; MERTK; PRKCSH; TESK2*), while 28 demonstrated a poor prognostic value (*AURKA; BUB1; BUB1B; CDC7; CDKN2C; CDKN3; CHEK1; CKS1B; CKS2; DBF4; DUSP10; HK2; PI4K2B; MAP2K6; MELK; NEK2; NTRK3; PAK2; PBK; PFKP; PLK4; PTPRG; RPRD1A; SRPK1; SRPK2; STK39; TK1; TTK*).

Analysis of their involvement in cellular physiology highlighted the cell cycle as the top KEGG pathway (Figure 1B), and string network of the 36 genes showed highly interconnected proteins particularly for those with a role in cell cycle (Figure 1C)

Hierarchical clustering underlined a spread expression of the genes among MM patients, except for a cluster composed of 14 kinases related to proliferation/mitosis (*CDKN2C; CDC7; CDKN3; BUB1B; MELK; BUB1; AURKA; NEK2; PBK; TTK; CHEK1; PLK4; CKS1B* and *TK1*), which exhibited a specific pattern of overexpression in a subgroup of patients (Supplementary Figure 1). Interestingly 10 of these 14 kinases are part of the CINSARC signature, associated with chromosomal instability in many cancer types including multiple myeloma[19].

Building a Kinome Index (KI) linked to the patient's outcome

We next combined the prognostic information of the 36 identified kinases in a GEP-based Kinome index (KI). This KI is the sum of the standardized expression value of

the 28 kinase genes associated with a poor prognostic value minus the sum of the standardized expression value of the eight genes associated with a favorable prognosis (Supplementary Figure 2). Maxstat algorithm segregated the HM cohort into two groups with 31% of the patients with a KI>2.1 and 69% of the patients with a KI≤2.1 with a maximum difference in overall survival (OS; Figure 2A). Patients with KI>2.1 have a median OS of 50.6 months versus not reached for patients with KI≤2.1 (p=1,7E-05)) and a median event free survival (EFS) of 20.1 months versus 40.6 months (p=4,5E-05) in the HM cohort (Figure 2B). The prognostic value of the KI was validated in the two additional independent UAMS-TT2 and TT3 cohorts for OS and EFS (Supplementary Figure 3).

KI is significantly higher in the proliferation (PR) and MAF MM molecular subgroups[20] known to be associated with a poor outcome (p<8E-18). Furthermore, higher KI was associated with the proliferating stages of B to plasma cell differentiation including activated B cells, pre-plasmablasts and plasmablasts compared to non-proliferating memory B cells and mature plasma cells (Figure 2D). This observation corroborates the association of the 36 kinases to cell cycle (Figure 1B) and the PR subgroup (Figure 2C), as well as the well-known association of kinases activation with proliferation. In addition, KI values increased with disease progression from normal Bone Marrow Plasma Cells (BMPC) to MM cells with a homogeneous index between the different cohorts tested (HM, TT2 and TT3) and HMCLs (p<0.01) (Figure 2D). Finally, we tested the KI in a cohort of 23 patients with paired samples at diagnosis and relapse, and identified a significant increase of the KI at relapse (p = 4E-04) (Figure 2E). Altogether these observations further highlight that the selected kinases comprising markers of genomic instability[19], could represent new potential therapeutic targets for high-risk MM patients.

KI kinases' inhibition leads to MM cell death *in vitro*

According to our *in silico* analysis the 36 genes demonstrated an outstanding connection with MM physiopathology and prognosis. Thus, we next assessed selected kinases of interest for their individual therapeutic potential on MM cells using specific inhibitors. In that purpose we first excluded the eight genes associated with favorable prognosis, and tested the 28 remaining kinases for their link with MM in literature. Three genes whose connections with MM were already widely studied

(more than 5 references identified in PubMed) (*CKS1B*[21]; *AURKA*[22]; *CDKN2C*[23]) were then also excluded, and we finally selected the seven kinases (*PBK; CHEK1; MPS1/TTK; CDC7-DBF4; MELK; PLK4; SRPK1*) that had commercially available specific inhibitors at the time of the study (Figure 3A). To note, all selected kinases are involved in the mitotic checkpoint (*PBK; MPS1/TTK; MELK; PLK4*) or replicative stress response (*CHK1; CDC7-DBF4; SRPK1*), and for all the selected kinases their expression are individually correlated to high-risk KI-defined MM subgroup (Supplementary Figure 4).

Then we assessed the kinase inhibitors for their potential anti-myeloma effect on four human myeloma cell lines (AMO-1, OPM2, XG-1 and XG-21). Remarkably all tested drugs led to a significant decrease in HMCLs viability and cell growth, with an IC50 indicated in Figure 3B (Supplementary Figure 5). We next investigated how the tested drugs impact cell death in the AMO1 HMCL using two drugs concentrations around the calculated IC50s. As shown on figure 3C, all drugs induced apoptosis as measured by the dramatic increase of annexin V and cleaved PARP staining following treatment. Interestingly, this effect was not observed at the lower concentration used, thus confirming our previous observation of a dose-dependent efficacy of the drugs. We then tested the ability of the kinase inhibitors to perturb cell-cycle progression. CHK1i, MELKi and CDC7-DBF4i are associated with a significant blockade of MM cells in S phase, while PLK4i and MPS1i induced a significant accumulation in G0/G1 in AMO1 HMCL (Supplementary Figure 6A and B). Thus, the different inhibitors tested here induced both apoptosis and deregulate MM cell proliferation. We also investigated the effect of PTPRG depletion using siRNA. PTPRG was shown to be spiked and mutated in MM[24]. Depletion of PTPRG results in significant decrease in MM cell growth together with apoptosis induction (Supplementary figure 15).

Next, we focused on the three inhibitors that induced MM cells toxicity at nanomolar concentration (CHK1i; MELKi; PLK4i) to validate their therapeutic interest using primary MM cells from patients co-cultured with their bone marrow microenvironment. Remarkably, all three tested drugs significantly reduced the number of tumor cells without toxicity for the bone marrow microenvironment (Figure 4A and Supplementary Figure 6C, D, E).

In addition, in order to demonstrate the capability of preclinical studies for the three selected inhibitors, we tested them in 5T33v cells, a murine model of multiple

myeloma[17]. As shown in figure 4B, CHK1i and MELKi demonstrated similar efficiency while PLK4i was less effective on 5T33vv cell viability compared to human myeloma cells.

Finally, using a proteome array we examined the pathways involved in apoptosis and cell cycle following treatments in AMO1 cells and in OPM2 cells that is p53 mutated[25]. For all three tested treatments we observed in AMO1, but as expected not in OPM2, an increased p53 phosphorylation on S15 (DNA damage response), S46 (apoptosis) and S392 (growth inhibition) (Figure 4C and Supplementary Figure 7). Other apoptotic markers including caspase 3 cleavage, p27, cytochrome C, HSP60, TRAIL, Bad and Bcl-x were also induced. Upon CHK1i treatment in AMO1, we also observed a decrease in Claspin and Survivin levels, two proteins involved in cell cycle and replication that have been linked to the CHK1 pathway. Indeed Claspin is a co-activator of CHK1[26,27], whereas Survivin degradation depends on the XAF1/XIAP1[28] a pro-apoptotic complex involved in CHK1 degradation[29]. Those effects were not observed in OPM2 cells although we observed an increase of the pro-apoptotic proteins Diablo and FADD and a decreased in the proliferation related proteins TOR and P70 S6 kinases[30]. Heterogeneity of the cell lines regarding the p53 status could explain these differences. However, in both tested cell lines anti, and pro-apoptotic signals were deregulated. Altogether, these data demonstrate the pro-apoptotic and anti-proliferative effects of these three molecules in MM cells and highlight the potential of these kinases as new therapeutic targets in high-risk MM patients.

Conventional MM therapies are potentialized by selected kinase inhibitors.

We then investigated the therapeutic interest of combining these kinase inhibitors with therapeutic drugs commonly used in MM (e.g. Melphalan, Lenalidomide, Velcade). Combining sub-lethal IC20 for all the kinase inhibitors with increasing concentrations of standard agents allowed us to identify a significant potentialization of Melphalan toxicity by CHK1, MELK, PBK and CDC7-DBF4 inhibitors in at least two out of the four HMCLs investigated. However, no significant effect on the calculated IC50 was noticed for the co-treatment of Melphalan with PLK4, MPS1 and SRPK1 inhibitors with a potential calculated antagonism of the two molecules (Figure 5A and Supplementary Figure 8A). For the immunomodulatory agent Lenalidomide, no significant effect was observed with the tested combinations in two Lenalidomide

resistant HMCLs XG1 and XG21. However, the effect of Lenalidomide was significantly potentialized in two other HMCLs (AMO1 and OPM2) in combination with the CHK1, MELK or PBK inhibitors. Remarkably, addition of CHK1i, MELKi or PLK4i could overcome Lenalidomide resistance of the AMO1 cell line (Figure 5B and Supplementary Figure 8B). Conversely, we could not observe any synergy or even additivity for the co-treatment with Velcade, whatever the cell line tested or the kinase inhibitor used (Supplementary Figure 9A). Altogether these results demonstrate the therapeutic interest of CHK1i, MELKi, CDC7-DBF4i and PBKi in combination with Melphalan and IMiDs in MM (Supplementary Figure 9B).

To characterize the mechanisms involved, we monitored apoptosis after co-treatments of kinases inhibitors with Melphalan or Lenalidomide in AMO1 and OPM2 cells. Sub-lethal dose of Melphalan or Lenalidomide were used in combination with the calculated IC20 of the kinase inhibitors. CHK1i, MELKi and CDC7-DBF4i increased cell death via apoptosis when cells were co-treated with Melphalan or Lenalidomide. In addition, PLK4i co-treatment only potentialized cell death with Lenalidomide (Figure 6A and Supplementary Figure 10A). As expected from cell growth analyses, SRPK1i and MPS1i did not increase cell death (Supplementary Figure 9C and Supplementary Figure 10A). Next, we monitored DNA damage by measuring levels of the DNA double-strand break (DSB) marker γH2AX after the different co-treatments. As expected, Melphalan treatment alone, even at the sub-lethal dose, increased the level of γH2AX, while Lenalidomide did not demonstrate any effect (Figure 6B and Supplementary Figure 10B). However, among all the combinations tested, only MELKi significantly potentialized Melphalan-induced DNA damage in AMO1 but not in OPM2 cells. Interestingly MELKi, CDC7-DBF4i and SRPK1i alone induced DSBs as monitored by γH2AX levels (Figure 6B and Supplementary Figure 9D) although it should be noticed that high concentration of the CHK1 inhibitor AZD7762 or MELK inhibitor OTSSP167 induce early DSB that progressively decrease as monitored by measuring γH2AX in AMO1 after 24 and 48 hours of treatment (Supplementary Figure 11). Thus, the significant potentialization of Melphalan and Lenalidomide toxicity by CHK1i, MELKi, CDC7-DBF4i and SRPK1i appears to be due to an increased induction of apoptosis, and not particularly to an increase of DNA damage or cell cycle deregulation (Supplementary Figure 12).

According to these results, we investigated the therapeutic interest of kinases inhibitors to overcome Melphalan resistance using Melphalan resistant (Mres) XG7 and XG2 cell lines (Figure 7A and Supplementary Figure 13A). Interestingly, while no clear differences could be observed for the IC50 of MELKi, CHK1i, PBKi and MPS1i in the Mres and sensitive (WT) cell lines, PLK4i and CDC7-DBF4i demonstrated a significantly higher toxicity in the XG7 Mres cell line (Figure 7B) but not in XG2 Mres HMCL (Supplementary Figure 13B). Sublethal IC20 of CHK1i, PBKi and CDC7-DBF4i overcame Melphalan resistance of both cell lines tested (Figure 7C and Supplementary Figure 13C), while the other inhibitors tested did not show a significant effect. It should however be underlined that the inhibitors alone are active on both resistant and sensitive cell lines as shown on Figure 7B and Supplementary Figure 13B. Thus, our results highlight the therapeutic interest of CHK1i, MELKi, CDC7-DBF4i and SRPK1i used alone or in combination with conventional therapies, even in case of acquired resistance.

Discussion

Here we identified 36 kinases associated with a prognostic value in three independent cohorts of MM patients, allowing the creation of a kinase-related Gene Expression Profile (GEP) risk score (KI). Among them, CHK1, CDC7-DBF4, and MELK have been identified of therapeutic interest in MM[31–33]. PLK4, SRPK1, MPS1/TTK and PBK represent new therapeutic targets in MM. Using inhibitors of these seven kinases, we validated their therapeutic interest to target MM cells alone or in combination with conventional therapies. In addition, we also highlighted a list of protein kinases for which no inhibitor is currently available and represent promising new therapeutic targets at least in MM.

Our approach differs from a previous study exploiting a RNAi library to target the human kinome in six myeloma cell lines[8]. Surprisingly, only one kinase, *AURKA*, was selected in both studies. This discrepancy could reflect the fact that our study relies on the analysis of primary MM cells from patients and not on HMCLs as in previous studies. Since a large number of kinase (135/661) are differentially expressed between primary MM cells and HMCLs (Supplementary Table S3), we believe that our study provides a relevant view of the protein kinases important for the survival of MM cells.

Our Kinome Index is strikingly enriched in kinases involved in the progression through mitosis (PBK, PLK4, MELK, MPS1) and in the replication stress response (CHK1, CDC7-DBF4, SRPK1). These kinases are also enriched in proliferation[34] and proliferation GEP-based signatures, which represent also powerful risk factors in MM[10,35]. Although the 36 genes of the KI only have a limited overlap with these signatures indicating that KI does not simply reflect a higher cell proliferation index.

Among the inhibitors against targets validated here (CHK1, MELK, PLK4, SRPK1, CDC7-DBF4, MPS1/TTK and PBK), the CHK1 inhibitor AZD7762 was of particular interest due to its ability to act alone or in combination with other drugs. Our results differ from two earlier studies reporting a limited toxicity of AZD7762 on HMCLs at doses equivalent of our calculated IC50, but at high Melphalan concentration, when combined with this drug[31,36]. These discrepancies could reflect differences in culture conditions, as in our hands, the drug sensitivity of HMCLs depends exquisitely on the confluency status at seeding and on the treatment protocol. Furthermore, we validated the therapeutic interest of CHK1i using primary MM cells from patients co-cultured with their bone marrow microenvironment, without detecting significant

toxicity on non-myeloma cells. Our observations greatly implement the previous studies, either on the activity of the molecule alone, in combination with Melphalan and IMiDs, or to overcome MM drug resistance.

The MELK inhibitor OTSSP167 also demonstrated therapeutic interest. MELK is linked to multiple solid cancer types[37], and recently two groups showed the potential of this inhibitor in MM[33,38]. In addition to their work, we demonstrated the synergy between OTSSP167 with Melphalan and Lenalidomide and its interest to overcome Melphalan drug resistance. Interestingly, OTSSP167 off-targets' BUB1 and TTK/MPS1[39] are also part of our 36 selected kinases, which further highlight the potential of this inhibitor to target MM cells.

Our study represents the first attempt to investigate the therapeutic potential of PLK4, CDC7-DBF4, MPS1, PBK and SRPK1 inhibitors in MM, even though their effect on other cancer cell types has already been established[40–44]. All inhibitors did not demonstrated comparable effects, but they all showed MM cell toxicity at least when used alone. Furthermore, the toxicity of PLK4i was validated on primary MM cells, and synergy in MM apoptosis induction was also identified for PLK4i and CDC7-DBF4i when combined with Melphalan and Lenalidomide.

Remarkably, all the tested inhibitors (CHK1i, MELKi, PLK4i, SRPK1i, CDC7-DBF4i, MPS1/TTKi and PBKi) demonstrated anti myeloma activity by reducing viability and inducing cellular death of MM cells. Interestingly, a significant correlation between KI and response to PLK4i was identified (Supplementary Figure 15). The analysis of the potential mechanisms involved revealed that both cell cycle arrest and apoptosis contributed to the observed phenotype. Both intrinsic and extrinsic apoptosis pathways were involved for AZD7762, OTSSP167 and Centrinone B. Interestingly, these three inhibitors induced p53 pathway in AMO1, although we believe that the effect of these molecules is not exclusively p53 dependent since they similarly demonstrated significant toxicity in p53 proficient (XG1, OPM2) or p53 deficient (XG21, AMO1) MM cell lines. Though, considering AZD7762, this observation is surprising since several studies noted that CHK1 inhibitors were particularly toxic for p53-deficient cells[45] probably via the simultaneous abrogation of the G2 (CHK1) and G1 (p53) checkpoints, and initiation of mitotic catastrophe[31]. However, CHK1 can also suppress death pathways and therefore inhibition of CHK1 can reactivate apoptosis in a p53-independent fashion via caspase 2 activation, mitochondrial outer membrane permeabilization and cytochrome C release[46]. As cytochrome C induction

was observed for the three inhibitors tested, this last mechanism could explain the p53-independent effect, which implements considerably its therapeutic interest in MM, where p53 status is highly linked to prognosis.

Here, we demonstrated that low doses of CHK1, MELK, PBK and CDC7-DBF4 inhibitors were able to synergize or even reverse Melphalan resistance. This is very important considering that virtually all MM patients eventually relapse and develop drug resistance. These kinases have all been shown to decrease DNA damage tolerance[47–50], which could explain this observation. Similarly, CHK1, MELK and PBK inhibitors could overcome Lenalidomide resistance. Even if these observations are promising, additional *in vivo* experimentation are needed to confirm the potential and elucidate the mechanistic roles of these kinases in Lenalidomide and Melphalan resistance reversion.

The development of the Kinome index could be used to identify high-risk patients that could benefit from treatment with selected kinases inhibitors. Developing the KI, we also identified kinases that have already been linked to MM physiopathology including CKS1B[21], AURKA[22], CDKN2C[23], NEK2[51] and BUB1B[52]. In addition, we also identified numbers of kinases (PAK2, HK2, CDC7, BUB1, CKS2, TK1, MAP2K6, NTRK3, STK39, PTPRG, CDKN3, DUSP10, PFKP, SRPK2, RPRD1A, PI4K2B) without clear or documented connection with MM, but which are considered as potential targets in other cancers. According to the high degree of heterogeneity of the disease, we look forward to the development of new inhibitors targeting these kinases, which could be of therapeutic interest in MM.

To date, no kinase inhibitors have received the approval of the FDA for the treatment of MM[7]. Our study demonstrates that kinase targeting could be of therapeutic interest, especially in high-risk MM patients defined by the Kinome Index. Since this index significantly increase at relapse compared to newly diagnosed patients, CHK1, MELK, PLK4, SRPK1, CDC7-DBF4, MPS1/TTK and PBK inhibitors could represent new treatment options alone or in combination with Melphalan or IMiDs for refractory/relapsing MM patients.

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Authorship

Contribution: HdB designed and performed the research, analyzed the data, and wrote the paper; AB MJ AM CG EdB performed the research and analyzed the data; NR LV AS GC DH AK analyzed the data; PP analyzed the data and wrote the paper; JM designed and supervised the research and wrote the paper.

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The authors have no conflict of interest to declare.

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Figures Legends.

Figure 1: Identification of 36 kinome related probe sets linked to prognosis in three independent cohorts of newly diagnosed MM patients. A) Workflow analysis used to identify kinases with gene expression associated with a prognostic value in MM. Cohort 1 = HM-Montpellier cohort, Cohort 2 = UAMS-TT2, Cohort 3 = UAMS-TT3. Poor prognosis means that high gene expression is associated with a significant negative outcome, while Good prognosis means that high gene expression is linked to a better outcome; B) Reactome molecular signatures significantly enriched in the kinases related to a poor outcome in MM; C) String network of the 36 identified kinases. Red color represents cell cycle related kinases.

Figure 2: ***Prognostic value of the Kinome Index in MM***. A) Clustergram in the 206 HM cohort's patients (206 patients) of the 36 genes signal used to build the Kinome Index. Signals are displayed from low (deep blue) to high (deep red) expression; B) Patients of the HM cohort were ranked according to increased KI and a maximum difference in OS was obtained with KI of 2.1 splitting patients into high-risk (31%) and low-risk (69%) groups (OS and EFS); C) The KI was computed for MMCs of patients belonging to the subgroups of the University of Arkansas for Medical Science (UAMS) molecular classification of MM, using UAMS-TT2 cohort. Abbreviations: CD1: cyclin D1 and cyclin D3; CD2: cyclin D1 and cyclin D3; HY: hyperdiploid; LB: low bone disease; MF: c-MAF and MAFB; MS: MMSET; MY: myeloid; PR: proliferation; D) KI is increased in Pre-plasmablasts characterized by high proliferation during normal B to PC differentiation. MBC=Memory B cells (n=5); prePB= Pre-Plasmablast (n=5); PB= Plasmablast (n=5); LLPC= Long Live Plasma Cells (n=5); BMPC= Bone Marrow Plasma Cells (n=5); HM MM cohort (n=206); TT2 MM cohort (n=345); TT3 MM cohort (n=158); HMCLs= Human Myeloma Cell lines (n=44); E) KI is significantly higher at relapse compared to diagnosis in a cohort of 23 paired patient's samples (paired T-Test). p-value: *<0.05; **<0.01; ***<0.001.

Figure 3: Selected kinases inhibition induces human myeloma cell toxicity. A) Selection of 7 kinases for biological investigations based on citation report in Pubmed and the availability of inhibitors; B) IC50 of the different drugs in 4 HMCLs, and calculated IC20 for the AMO1 HMCL; C) Kinase inhibitors induce apoptosis (annexin

V and PARP cleavage) in AMO1 MM cell line at concentrations close to the calculated IC20 and IC50s; Annexin, and PARP cleavage, were monitored by flow cytometry after 4 days treatments. Results are representative of four independent experiments. Statistical significance was tested using a Student T-Test for pairs. p-value: *<0.05; **<0.01; ***<0.001.

Figure 4: Selected kinases inhibition induces human primary MM cell death and toxicity on 5TMM murine cells. A) Mononuclear cells from five patients with MM were treated or not with CHK1i, MELKi and PLK4i. At day 4 of culture, the viability and total cell counts were assessed and the percentage of $CD138^+$ viable plasma cells and bone marrow non-myeloma cells were determined by flow cytometry. Results are median values of the numbers of myeloma cells in the culture wells. Results were compared with a Student T-Test for pairs. B) Murine myeloma cell (5T33vv) viability was monitored by CTG after 24 and 48 hours treatment with CHK1i, MELKi and PLK4i. Results are representative of three independent experiments C) Apoptosis and Signaling pathways targeted by CHK1i, MELKi and PLK4i. Proteins accumulations were monitored after 48h treatment on AMO1 HMCL using proteome profiler array. Relative amount was calculated as the mean of pixel density. p-value: *<0.05; **<0.01; ***<0.001.

Figure 5: Kinase inhibitors enhance the sensitivity of MM cells to conventional treatments. HMCLs were cultured for 4 days in 96-well flat-bottom microtiter plates in RPMI 1640 medium, 10% fetal calf serum, 2 ng/ml IL-6 culture medium (control) and graded Melphalan concentrations (A) or Lenalidomide concentrations (B) in presence or absence of IC20 of CHK1i, MELKi, PBKi, CDC7-DBF4i, SRPKi, MPS1i and PLK4i. IC50s were calculated after viability assessment by CellTiter-Glo® Luminescent Cell Viability Assay. Results are representative of three independent experiments. p-value: *<0.05; **<0.01; ***<0.001. S=Significant synergy calculated by the method of Chou and Talalay.

Figure 6: Conventional MM therapies are potentialized by selected kinase inhibitors. Co-treatment with selected kinase inhibitors at IC20 and Melphalan or Lenalidomide. A) Apoptosis induction was analyzed using Annexin V APC staining by flow cytometry; B) DNA damage induction was analyzed measuring □H2AX levels;

Results are representative of four independent experiments. CI= Calculated Combination Index. Statistical significance was tested using a Student T-Test for pairs. p-value: *<0.05; **<0.01; ***<0.001. #=significantly different of each individual treatment.

Figure 7: Kinase inhibitors overcome resistance of Melphalan resistant MM cells. A) Dose response curves of XG7 WT and XG7 Melphalan resistant (MRes) cell lines; B) XG7 WT and XG7 MRes HMCLs were cultured for 4 days in 96-well flat-bottom microtiter plates in RPMI 1640 medium, 10% fetal calf serum, 2 ng/ml IL-6 culture medium (control) and graded Melphalan concentrations and selected kinase inhibitors at IC20. At day 4 of culture, the viability was assessed by CellTiter-Glo® Luminescent Cell Viability Assay. Data are mean values ± standard deviation (SD) of three independent experiments. p-value: *<0.05; **<0.01; ***<0.001 using a student T-Test for pairs.

Figure 8: Kinome expression profiling to define new therapeutic targets in Multiple Myeloma. The prognostic impact of the kinome expression was challenged in 3 independent cohorts of newly-diagnosed MM patients representing 709 patients. 36 clinically relevant genes were selected as potential therapeutic targets, and were used to create a Kinome Index with a strong prognostic value. Among the 36 selected kinases, we validated 7 kinases as new therapeutic targets in MM, as their related inhibitors presented therapeutic interest in MM for personalized treatments.

Figure 1

A

661 genes
Kinases related

Selection of genes asociated with prognosis in MM cohorts:

-104 genes in cohort 1 (Montpellier)
-72 genes in cohort 1 and cohort 2

-36 genes in three independent cohorts (cohorts 1, 2 and 3)

28 genes associated with poor prognosis

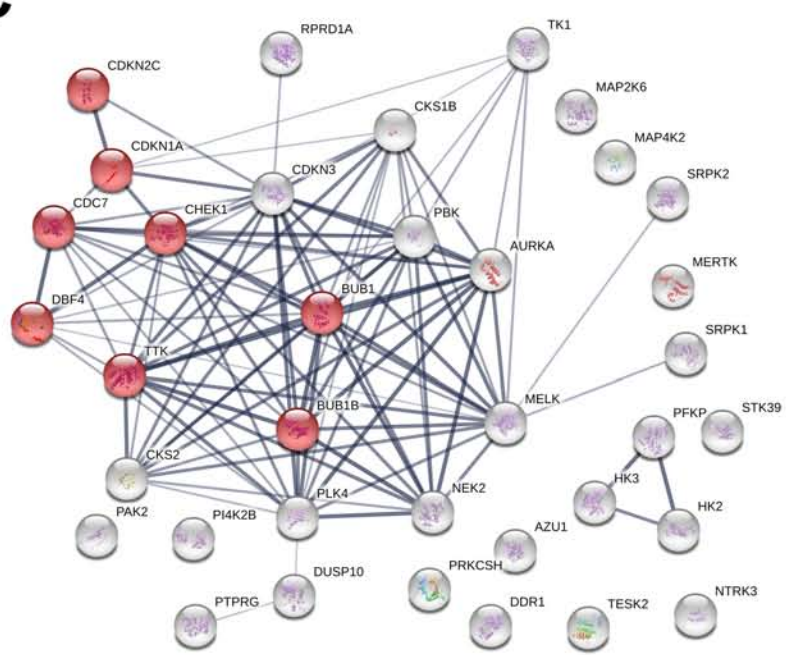
8 genes associated with good prognosis

B

KEGG pathways

#pathway ID	pathway description	observed gene count	false discovery rate
4110	Cell cycle	8	8.96e-09
51	Fructose and mannose metabolism	3	0.00215
52	Galactose metabolism	3	0.00215
524	Butirosin and neomycin biosynthesis	2	0.00215
10	Glycolysis / Gluconeogenesis	3	0.00918
1200	Carbon metabolism	3	0.0305
4010	MAPK signaling pathway	4	0.0305
4066	HIF-1 signaling pathway	3	0.0305
5166	HTLV-I infection	4	0.0305

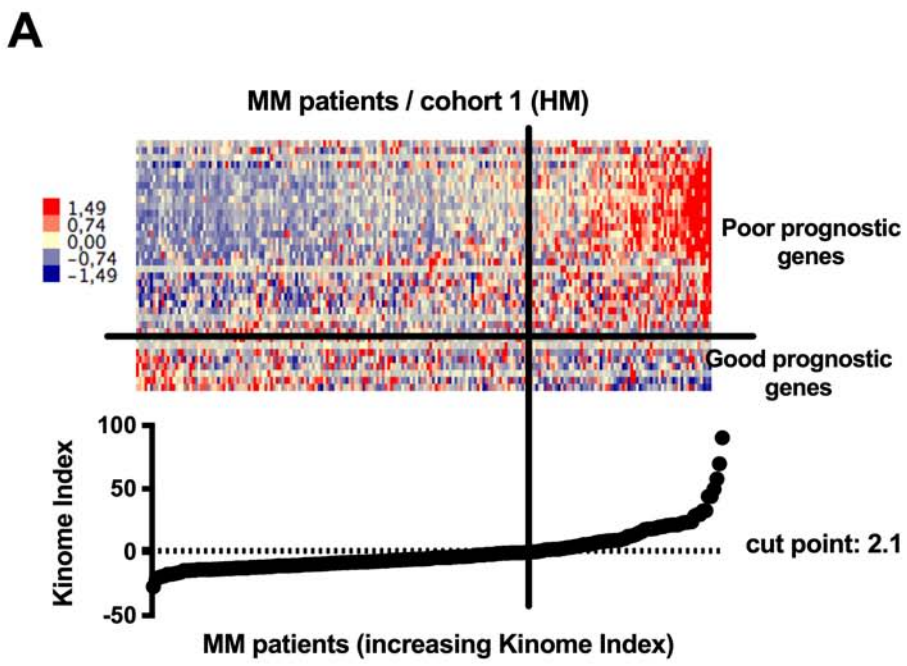
C

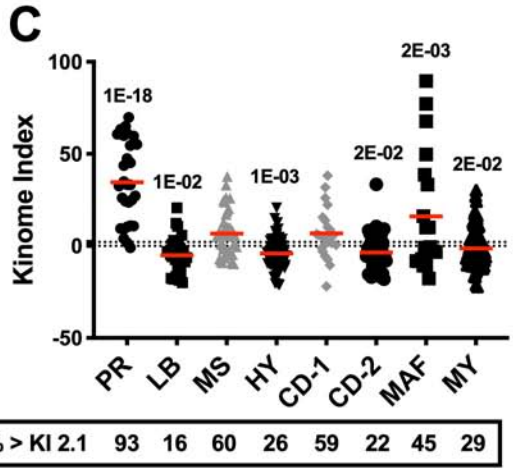


String network

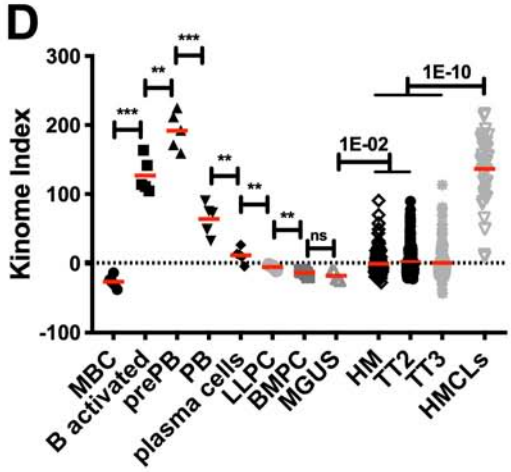
Figure 2

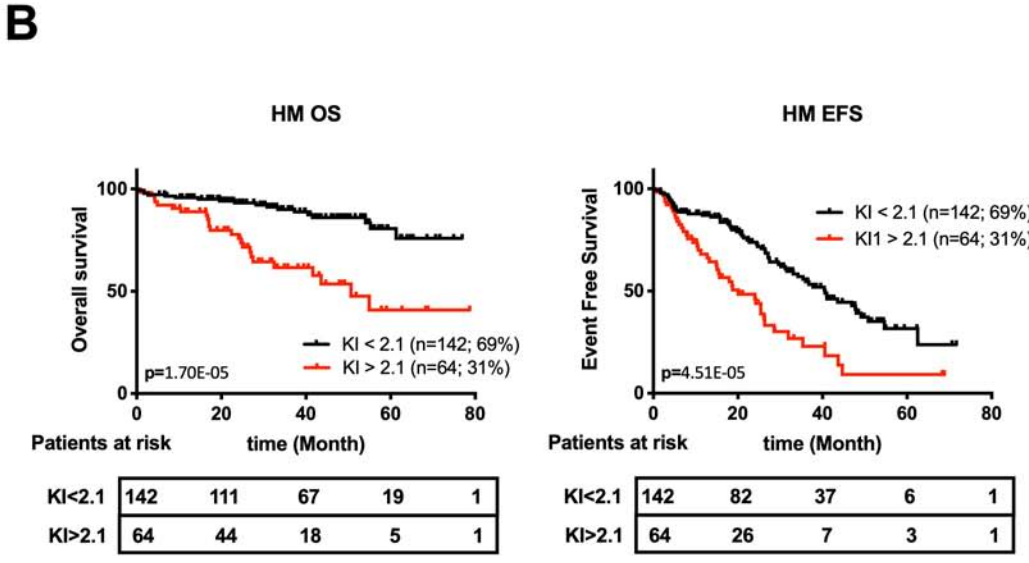
pvalue: *<0.05; **<0.01; ***<0.001





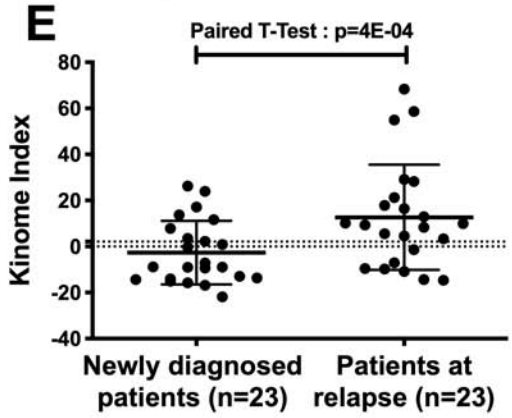
% > KI 2.1	93	16	60	26	59	22	45	29





KI<2.1	142	111	67	19	1
KI>2.1	64	44	18	5	1

KI<2.1	142	82	37	6	1
KI>2.1	64	26	7	3	1

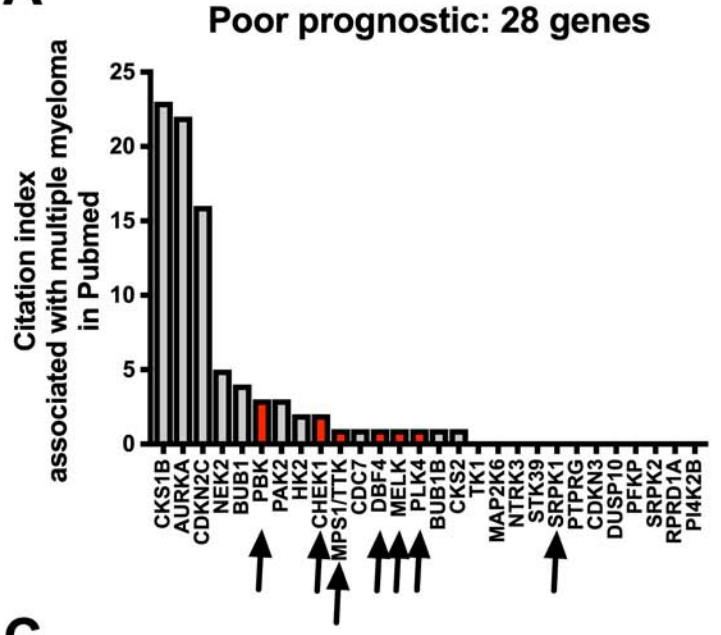


Longitudinal cohort with paired samples

Figure 3

pvalue: *<0.05; **<0.01; ***<0.001

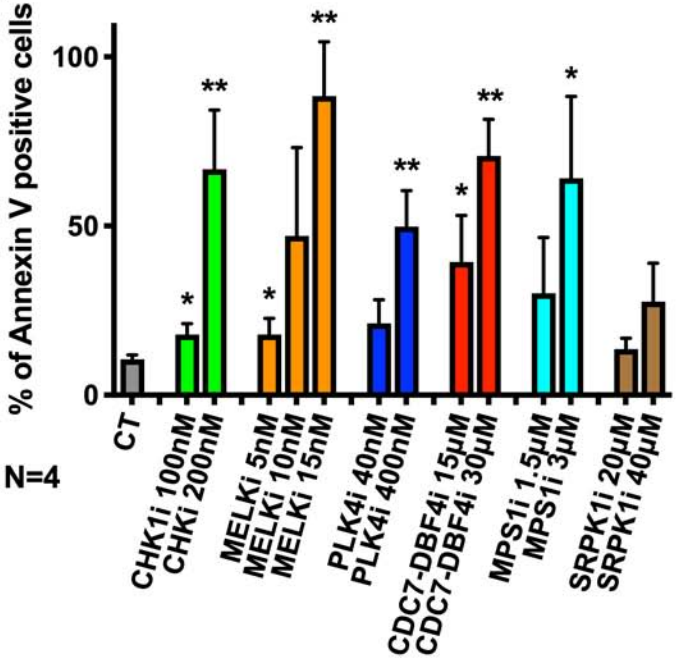
A



B

		AMO1	XG1	XG21	OPM2
CHK1i/AZD7762	IC50 nM	136	95	210	116
	IC20 nM	82	64	139	68
MELKi/OTSSP167	IC50 nM	8.2	12.5	2.2	15.7
	IC20 nM	5.4	7.8	1.0	7.0
PLK4i/Centrinone B	IC50 nM	421	226	1392	340
	IC20 nM	24	4	127	27
PBKi/HI-TOPK	IC50 µM	5.1	4.4	4.1	5.0
	IC20 µM	3.9	2.8	3.1	3.3
CDC7-DBF4i/XL413	IC50 µM	19.9	4.2	30.3	24.5
	IC20 µM	9.4	1.3	13.7	7.0
MPS1i/AZ3146	IC50 µM	2.6	1.2	3.0	1.9
	IC20 µM	1.5	0.8	1.5	1.1
SRPK1i/SRPIN340	IC50 µM	43	30	26	33
	IC20 µM	30	17	15	20

C



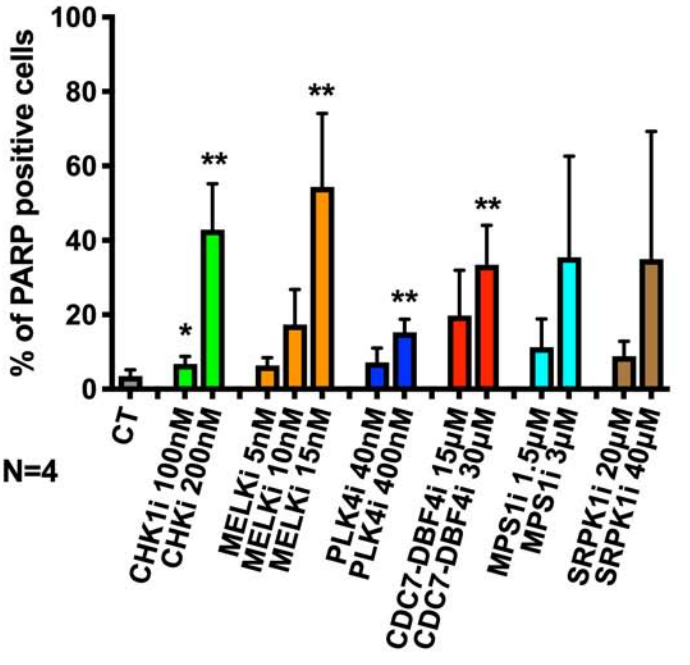


Figure 4

pvalue: *<0.05; **<0.01; ***<0.001

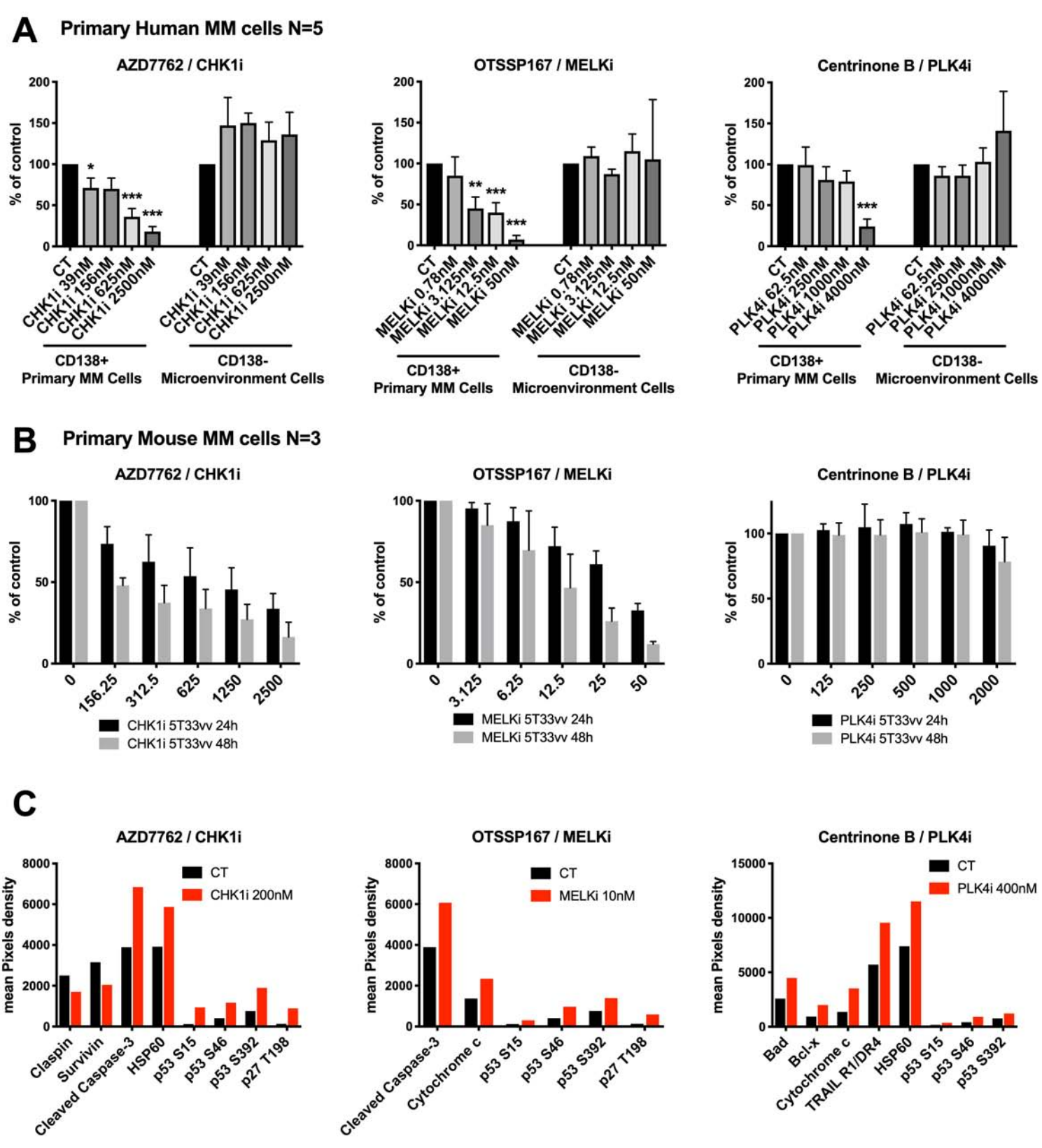


Figure 5

pvalue: *<0.05; **<0.01; ***<0.001

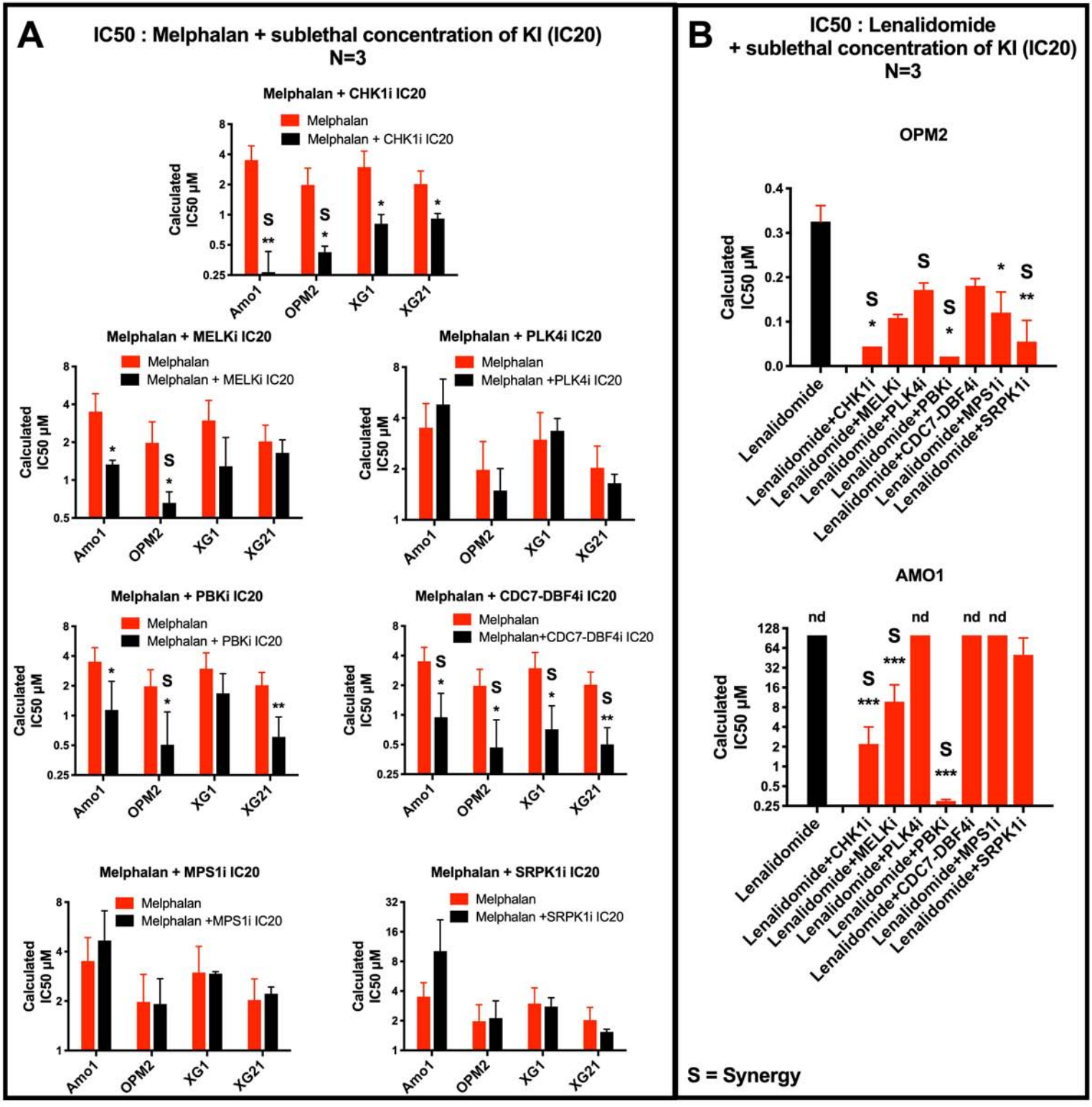


Figure 6

pvalue: *<0.05; **<0.01; ***<0.001
#=significantly different of each individual treatment

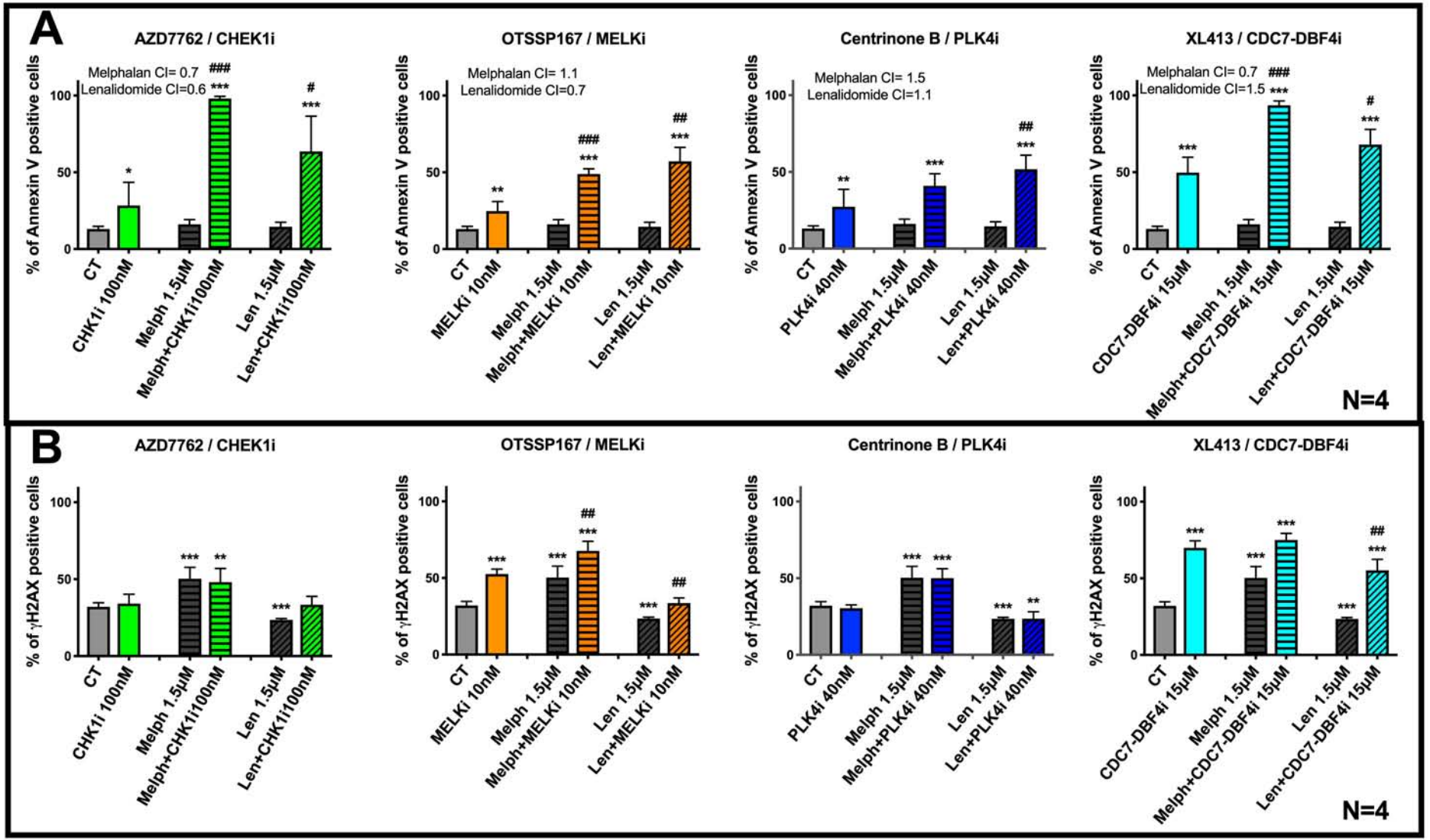
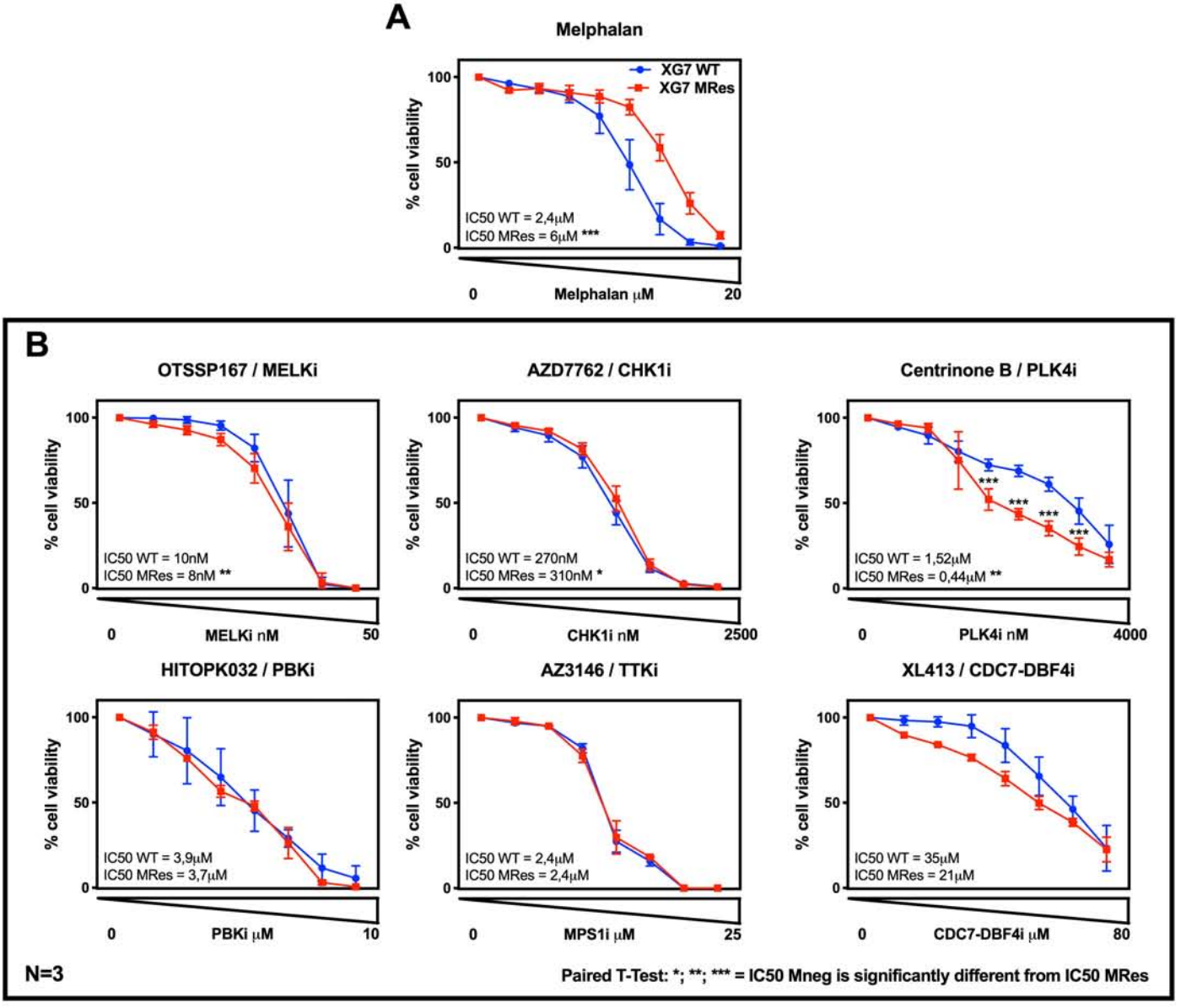
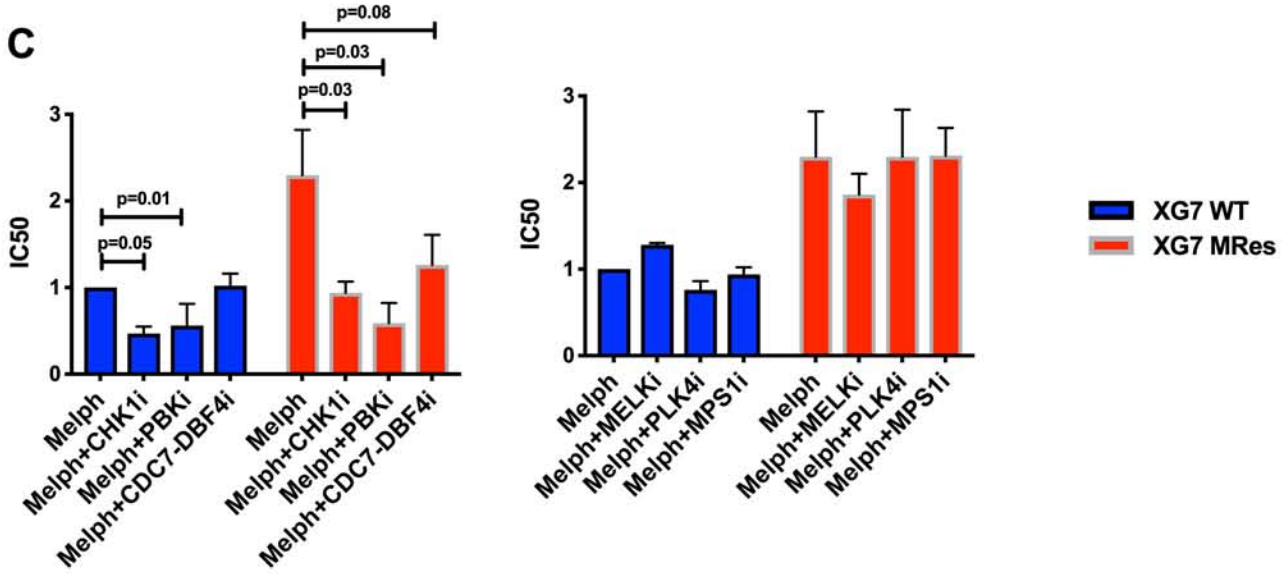


Figure 7

pvalue: *<0.05; **<0.01; ***<0.001



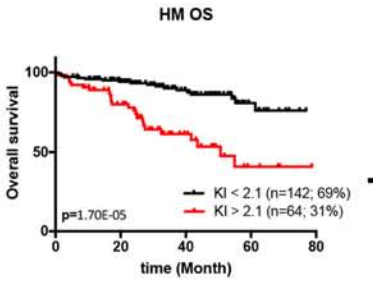


Kinome expression profiling to target new therapeutic avenues in Multiple Myeloma

709 Human MM samples

Gene expression profiles

Kinome Analysis



36 Clinically relevant kinases

→ **potential therapeutic targets**

Kinome index

Therapeutic marker

Sensitivity

Resistance

Kinase inhibitors

Targeting MM

7 new kinases related targets

(available inhibitors) **:**

CDC7-DBF4; CHEK1; MELK; MPS1; PBK/TOPK; PLK4; SRPK1

- MM cell cytotoxicity
- Synergy with Melphalan and IMiDs
- Overcome resistance to Melphalan and IMiDs

Supplementary experiment procedures

Kinome Index

A list of 661 genes of kinases or kinases related have been extracted from literature[9], and challenged in the HM cohort for OS prognostic values The prognostic value of each of the genes was computed using maximally selected rank test from R package MaxStat. After Benjamini Hochberg multiple testing correction a list of 104 significant prognostic genes has been extracted. This second list has then been challenged for similar prognosis value in the UAMS-TT2 validation cohort. 72 genes were thus extracted that have been then challenged for similar prognostic value in the UAMS-TT3 second validation cohort. A final list of 36 genes was then obtained representing genes associated with similar prognostic values in the three cohorts. Each pset value was standardized and the Kinome Index (called KI) was built using the following equation: KI= Σ(Poor prognosis gene standardized expression) – Σ(Good prognosis gene standardized expression). Maxstat analysis of the KI in HM cohort determined a cutoff of 2.1, with KI>2.1 is associated with poor prognosis and KI<2.1 is associated with good prognosis.

Cell cycle, DNA damage and apoptosis analysis

Cells were culture in 12 wells plate for 4 days. Apoptotic cells were detected using phycoerythrin-conjugated Annexin V (PE-annexin V, BD Pharmingen). For the cell cycle and DNA damage, we used the Apoptosis, DNA damage and cell proliferation kit (BD Pharmingen), following the manufacturer's protocol.

Proteome ARRAY

Phospho kinases and apoptosis proteins were quantified using the dedicated proteome Profiler™ array (RD systems, Bio-techne) following the manufacturer instruction. 500µg and 300µg protein were used for the two arrays respectively.

Combination Index and statistics

Statistical comparisons were done with unpaired or paired Student's t-tests. The effect of drug combination was evaluated using the methods developed by Chou and Talalay[18] by calculating the combination Index (CI), with $CI < 1$, $CI = 1$, and $CI > 1$

respectively indicating synergism, additive effects, and antagonism. Here we used CI= 0.90–1.10 to indicated additivity.

Supplementary figure legends:

Supplementary Figure 1: Hierarchical clustering in HM cohort demonstrates a heterogeneous profile of expression for the 36 kinase genes related to adverse outcome in MM.

Supplementary Figure 2: Building a Kinome Index based on the expression of the 36 kinase related genes.

Supplementary Figure 3: KI is associated with a poor prognosis (OS and EFS) in an independent cohort of 345 patients (UAMS-TT2 cohort) (A and B), and is associated with a poor prognosis in UAMS-TT3 cohort (N = 158) (C).

Supplementary Figure 4: Kinases expression in Low and High-risk group show correlation between prognosis and kinases gene expression.

Supplementary Figure 5: HMCLs viability was assessed by CellTiter-Glo® Luminescent Cell Viability Assay after treatments with all kinase inhibitors in 4 different HMCLs (AMO1, OPM2, XG1, XG21). Cell viability is expressed in % of untreated condition. N=3

Supplementary Figure 6: A) Kinase inhibitors leads to defects in cell cycle progression in AMO1 cell line. After 4 days of treatment, AMO1 cell cycle was analyzed using BrdU incorporation and labelling with an anti-BrdU antibody and DAPI. Data are mean values ± standard deviation (SD) of three independent experiments; B) Percentage of $CD138^{+}$ MM cells after treatment by AZD7762, OTSSP167 and Centrinone B in primary MM samples from 5 patients. p-value: *<0.05; **<0.01; ***<0.001.

Supplementary Figure 7: Apoptosis and Signaling pathways targeted by CHK1i, MELKi and PLK4i. Proteins accumulations were monitored after 48h treatment on OPM2 HMCL using proteome profiler array. Relative amount was calculated as the mean of pixel density.

Supplementary Figure 8: HMCLs viability was assessed by CellTiter-Glo® Luminescent Cell Viability Assay in 4 HMCLs after co-treatment with selected kinase inhibitors at IC20 and A) Melphalan or B) Lenalidomide. Cell viability is expressed in % of untreated condition. Results are representative of three independent experiments

Supplementary Figure 9: A) Co-treatment with selected kinase inhibitors at IC20 and Velcade. Cell viability was assessed by CellTiter-Glo® Luminescent Cell Viability Assay; B) Combination Index (CI) for co-treatment of Melphalan or Lenalidomide with the kinase inhibitors in 4 HMCLs. C) Apoptosis induction was analyzed using Annexin V APC staining by flow cytometry; D) DNA damage induction was analyzed measuring $_{\gamma}$H2AX levels E) Cell cycle, following SRPIN340 and AZ3146 co-treatment in AMO1 cell line, was analyzed using BrdU incorporation and labelling with an anti-BrdU antibody and DAPI. Data are mean values ± standard deviation (SD) of four independent experiments. p-value: *<0.05; **<0.01; ***<0.001 using a Student T-Test for pairs.

Supplementary Figure 10: Conventional MM therapies are potentialized by selected kinase inhibitors in OPM2 cell line. Co-treatment with selected kinase inhibitors at IC20 and Melphalan or Lenalidomide. A) Apoptosis induction was analyzed using Annexin V APC staining by flow cytometry; B) DNA damage induction was analyzed measuring $_{\gamma}$H2AX levels; Results are representative of four independent experiments. CI= Calculated Combination Index. Statistical significance was tested using a Student T-Test for pairs. p-value: *<0.05; **<0.01; ***<0.001. #=significantly different of each individual treatment

Supplementary Figure 11: Kinases inhibitors induce early DNA damage as monitored by Western Blot to follow $_{\gamma}$H2AX levels in AMO1 cell line after 24h or 48h treatment. Melphaln was used as positive control of DNA damage induction.

Supplementary Figure 12: Conventional MM therapies combined with selected kinase inhibitors induce defects in cell cycle progression. Combination of Melphalan or Lenalidomide with A) AZD7762; B) OTSSP167; C) Centrinone B; D) XL413 have been tested. HMCL cell cycle was analyzed using BrdU incorporation and labelling with an anti-BrdU antibody and DAPI. Data are mean values ± standard deviation (SD) of four

independent experiments. p-value: *<0.05; **<0.01; ***<0.001 using a Student T-Test for pairs.

Supplementary Figure 13: Kinase inhibitors overcome resistance of Melphalan resistant XG2 cell line. A) Dose response curves of XG2 WT and XG2 Melphalan resistant (MRes) cell lines; B) XG2 WT and XG2 MRes HMCLs were cultured for 4 days in 96-well flat-bottom microtiter plates in RPMI 1640 medium, 10% fetal calf serum, 2 ng/ml IL-6 culture medium (control) and graded Melphalan concentrations and selected kinase inhibitors at IC20. At day 4 of culture, the viability was assessed by CellTiter-Glo® Luminescent Cell Viability Assay. Data are mean values ± standard deviation (SD) of three independent experiments. p-value: *<0.05; **<0.01; ***<0.001 using a student T-Test for pairs.

Supplementary Figure 14: PTPRG depletion reduces cell proliferation in OPM2 cell line. OPM2 HMCL was culture at 0.1 x 10^6 cell/ml with 200nmol siRNA (ON-TARGETplus Human PTPRG smart pool or ON-TARGETplus Non-targeting Pool, Dharmacon) and lipofectamine (Thermo Fisher scientific). After 4 days, cell viability was measured using trypan blue exclusion method and apoptotic cells were detected using phycoerythrin-conjugated Annexin V (PE-annexin V, BD Pharmingen). PTPRG gene expression was assessed by qPCR using a taqman specific probe targeting PTPRG (hs00892788_m1, Thermo Fisher scientific). p-value: *<0.05

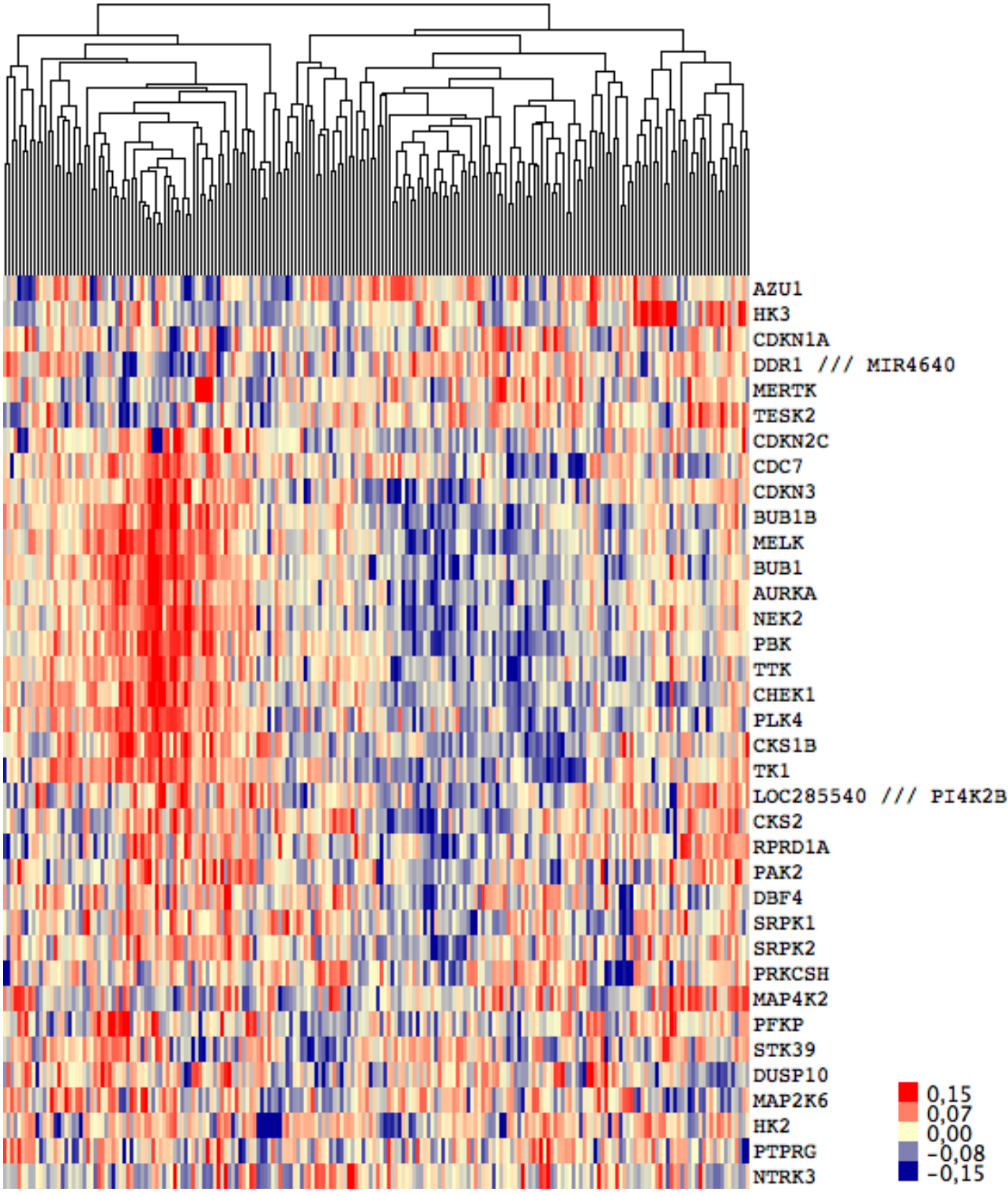
Supplementary Figure 15: High KI is significantly correlated to PLK4i response in MM cells.

Supplementary Table S1: list of kinases related probesets (from Sabatier R. et al. Kinome expression profiling and prognosis of basal breast cancers. Mol. Cancer 10, 86 (2011). Reference 10)

Supplementary Table S2: list of the 36 selected probesets and their prognostic values in HM UAMS-TT2 and UAMS-TT3 cohorts.

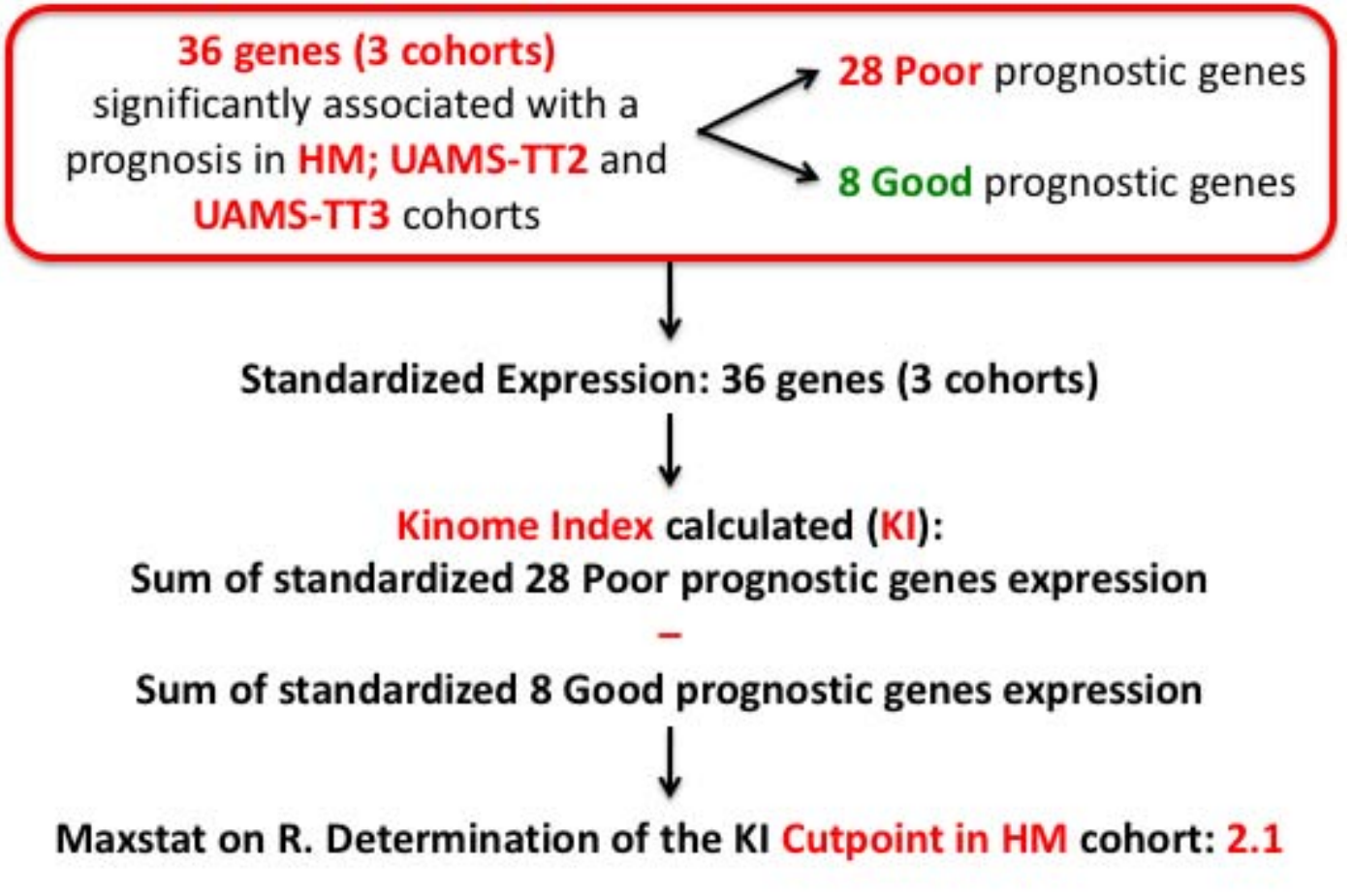
Supplementary Table S3: 135 kinases differentially expressed in HM and HMCLs, identified with SAM (Significance Anlaysis of Microarray) methods

Supplementary Figure 1

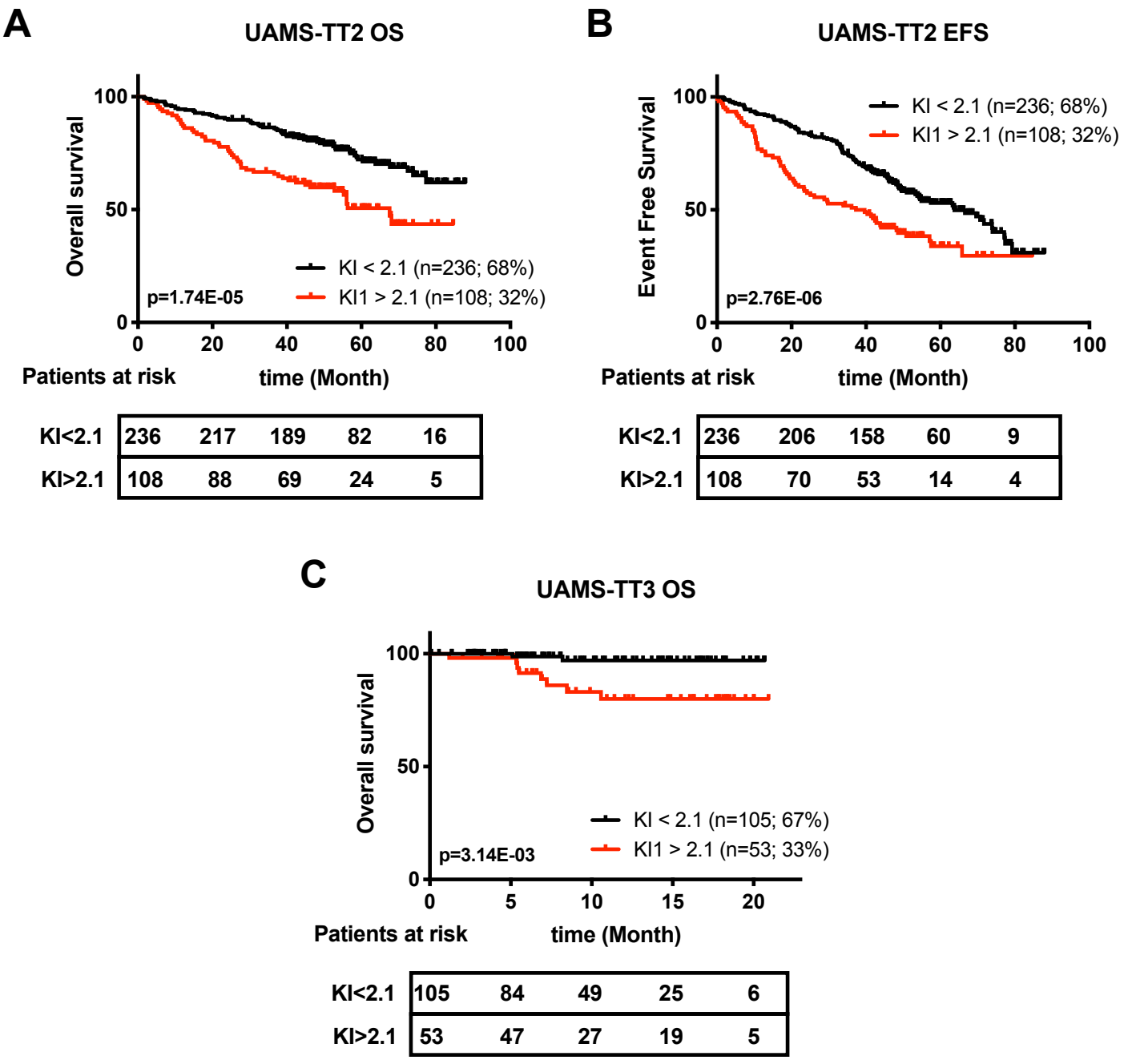


36 psets; HM cohort hierachical clustering

Supplementary Figure 2
Building a Kinome Index

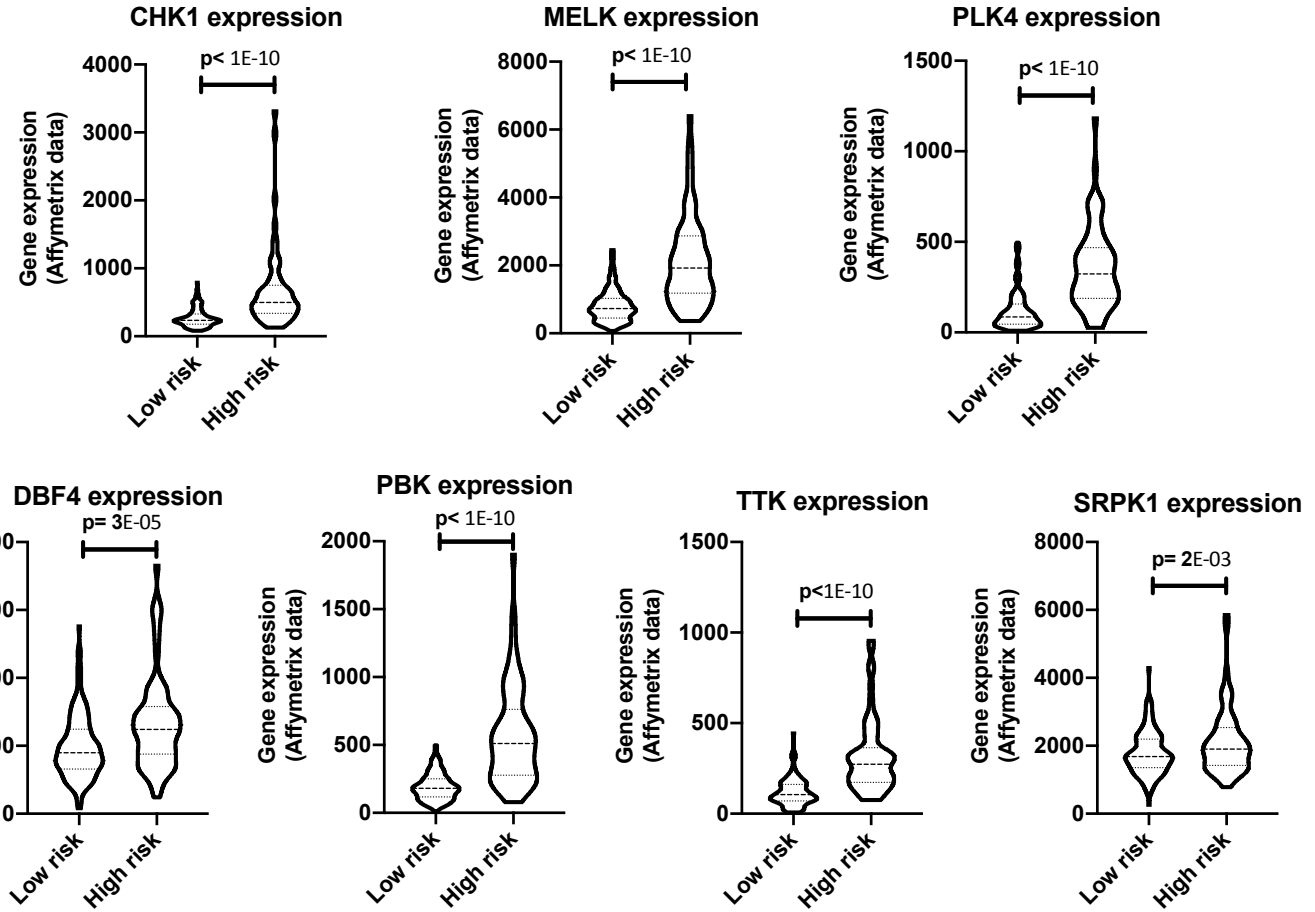


Supplementary Figure 3

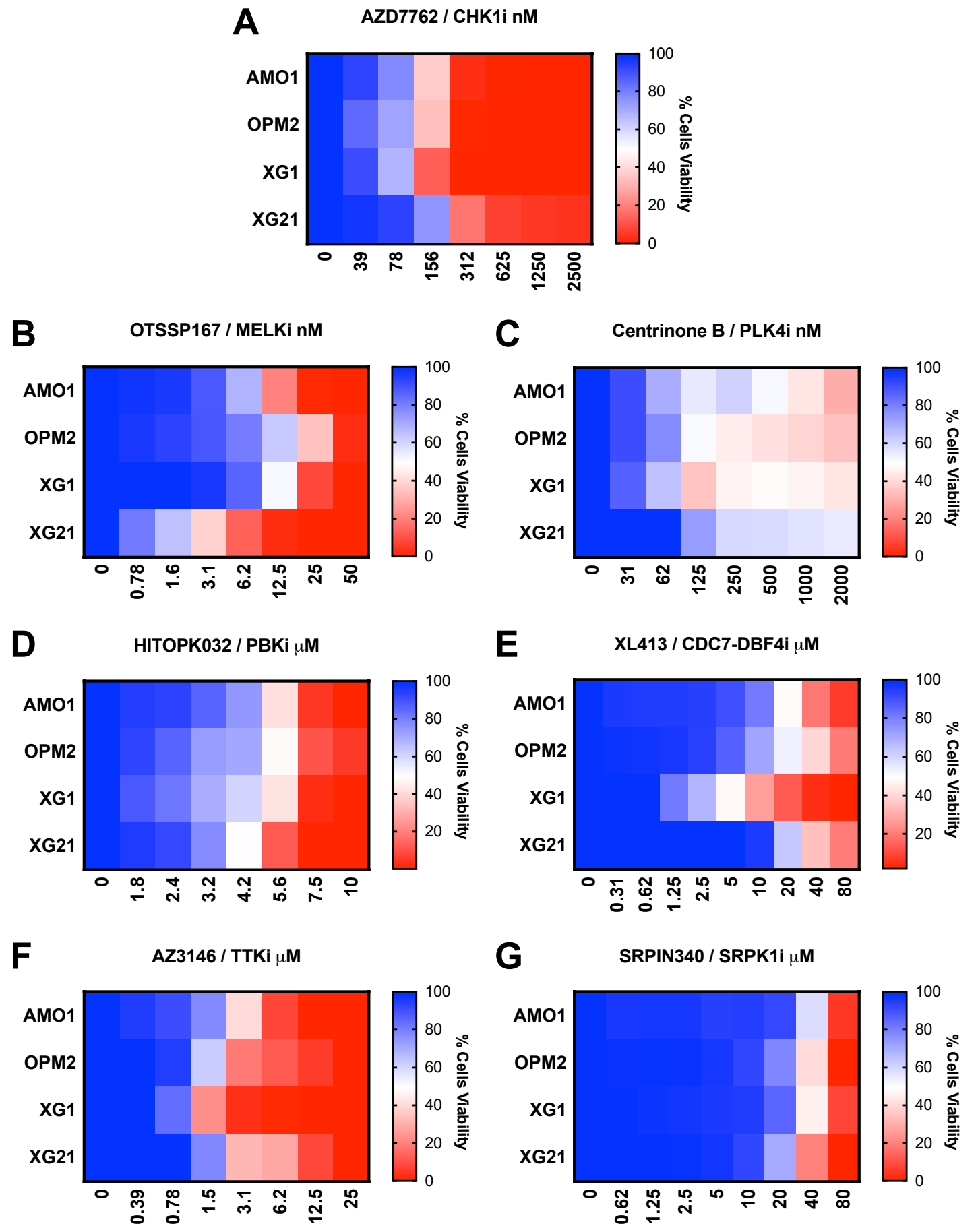


Supplementary Figure 4

Kinases expression in Low and High risk groups show correlation between prognosis and expression.

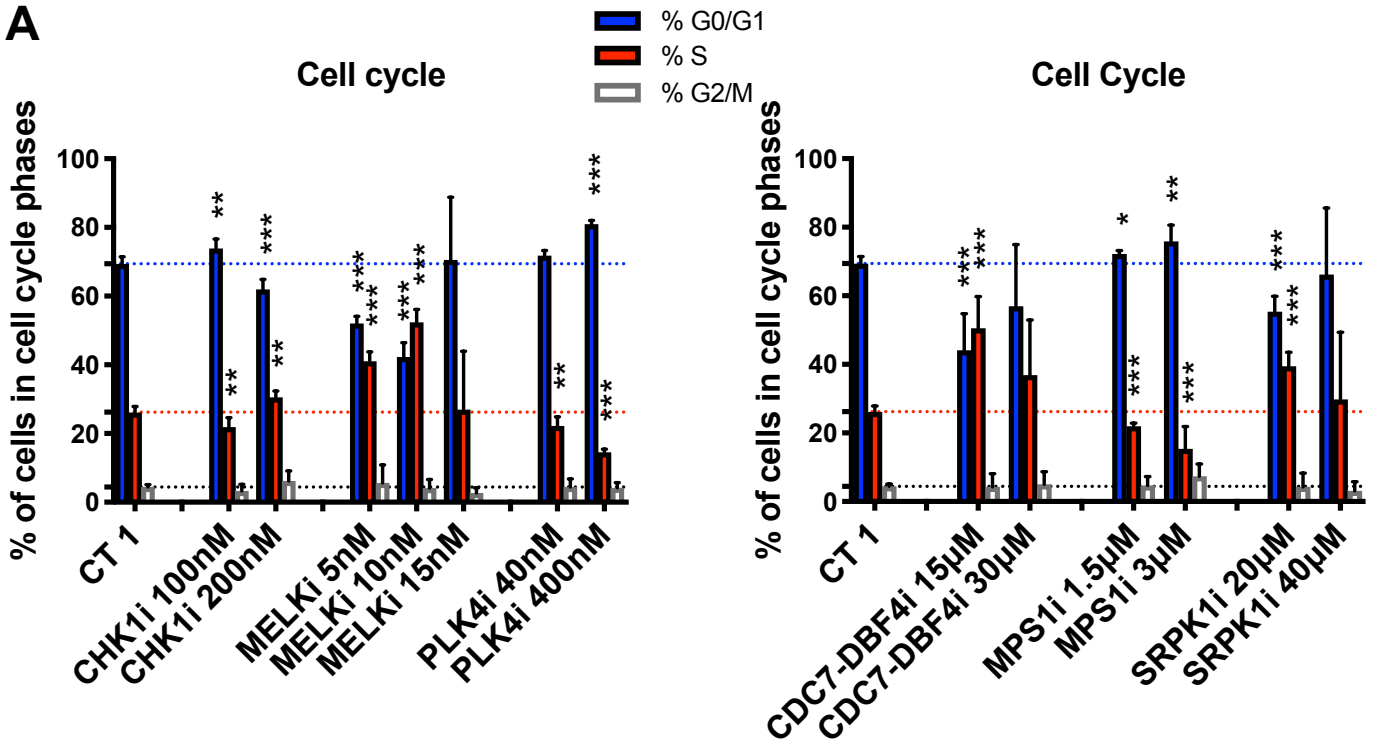


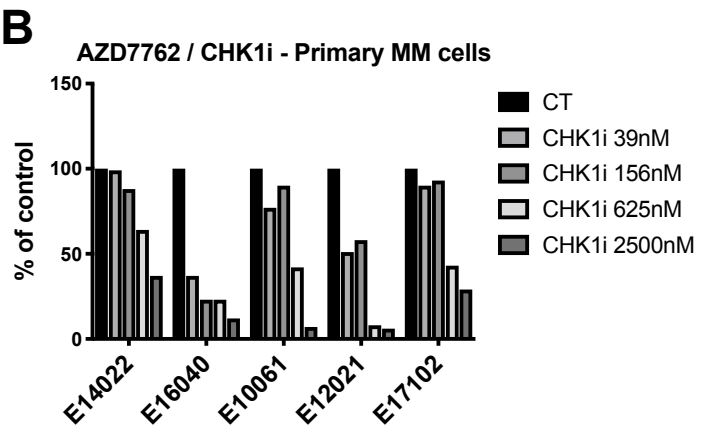
Supplementary Figure 5

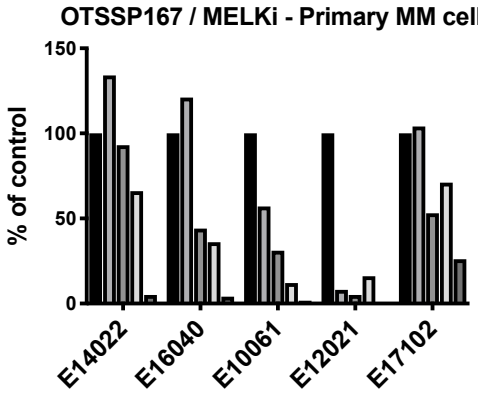


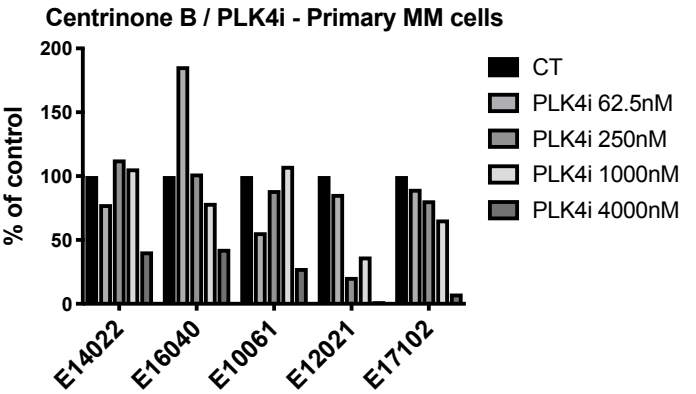
Supplementary Figure 6

pvalue: *<0.05; **<0.01; ***<0.001

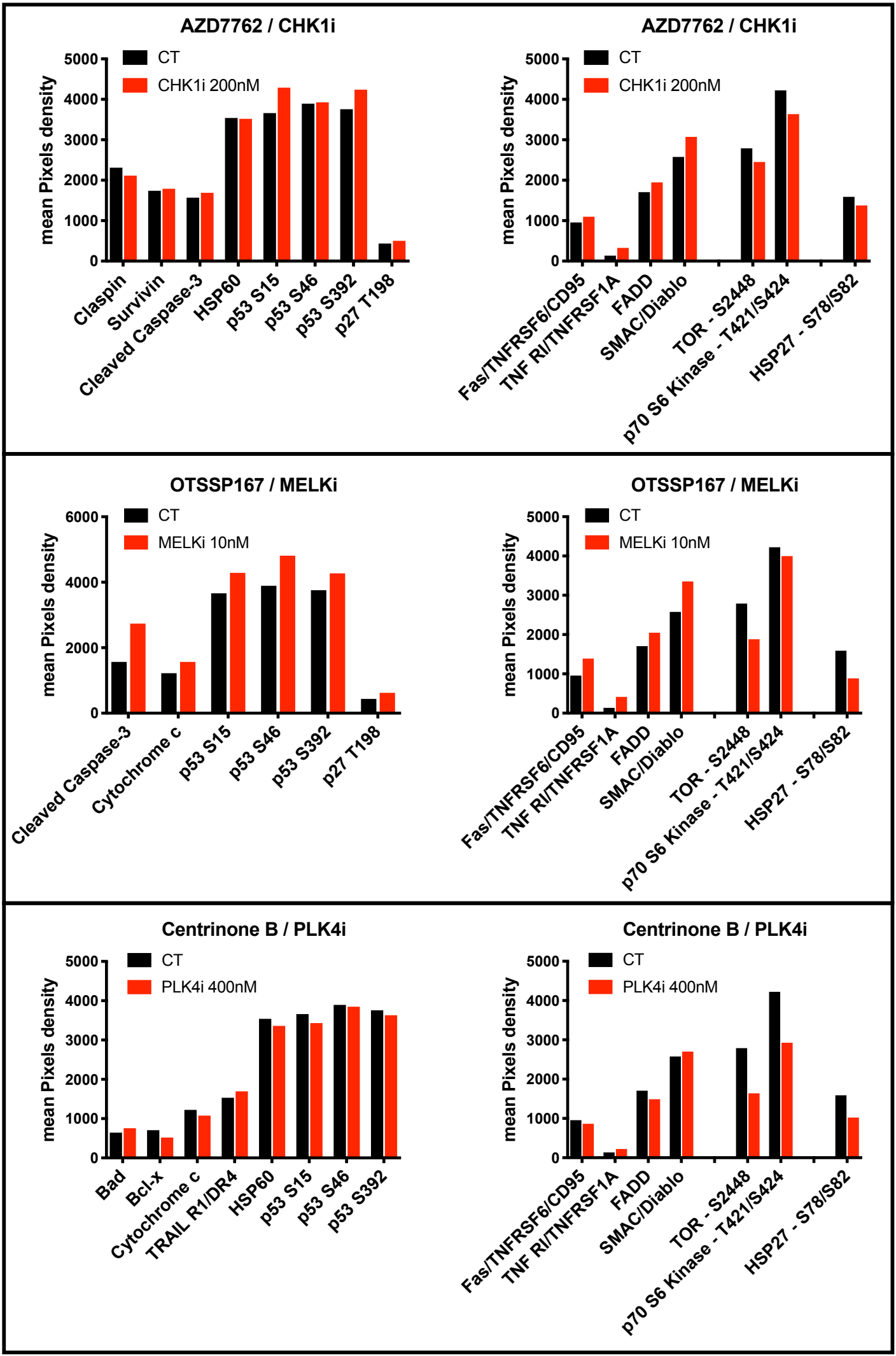




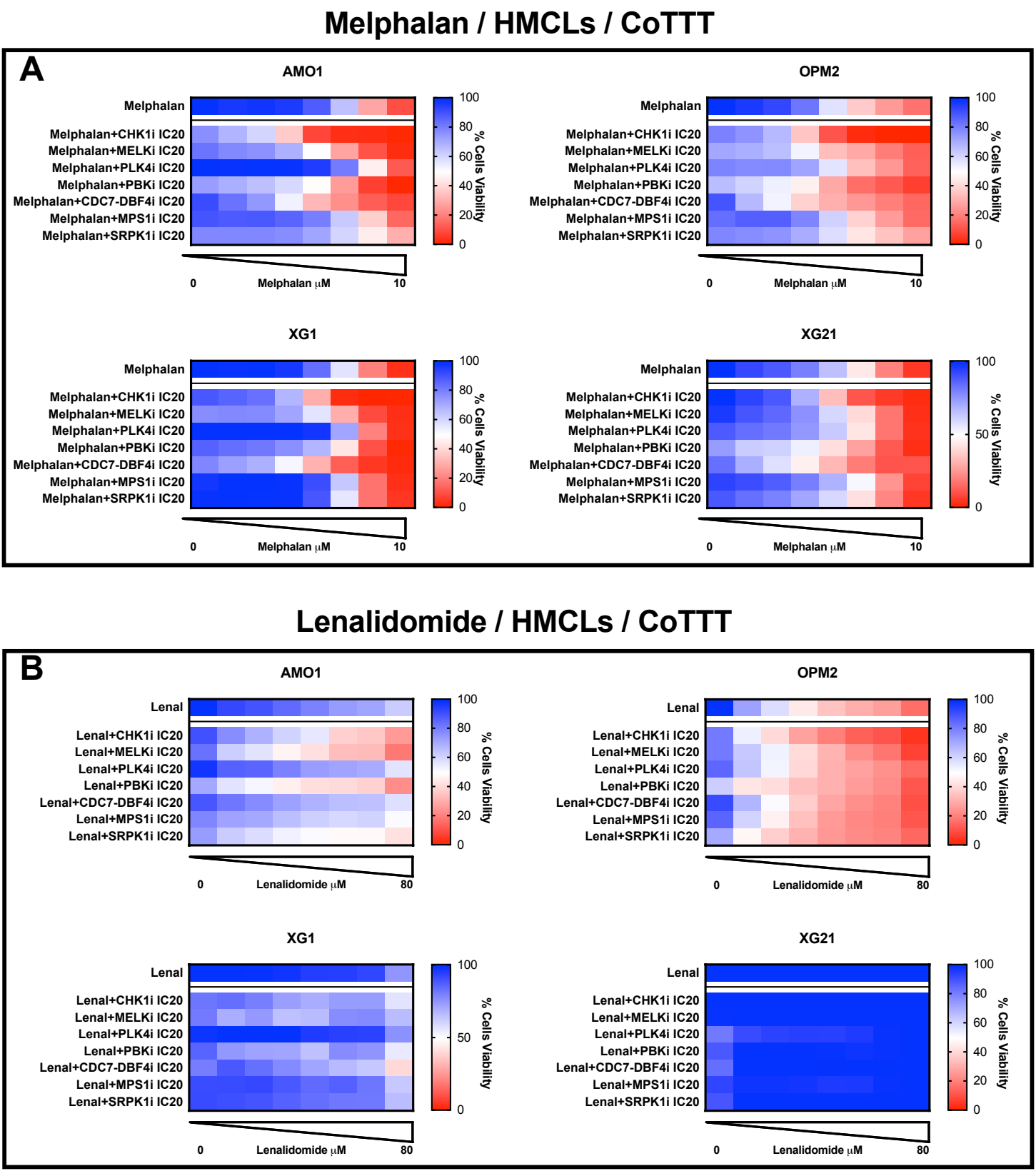




Supplementary Figure 7 proteome OPM2 cell line



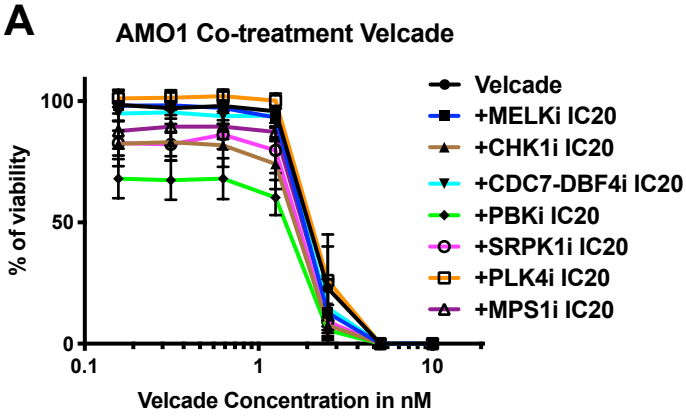
Supplementary Figure 8



Supplementary Figure 9

pvalue: *<0.05; **<0.01; ***<0.001

A

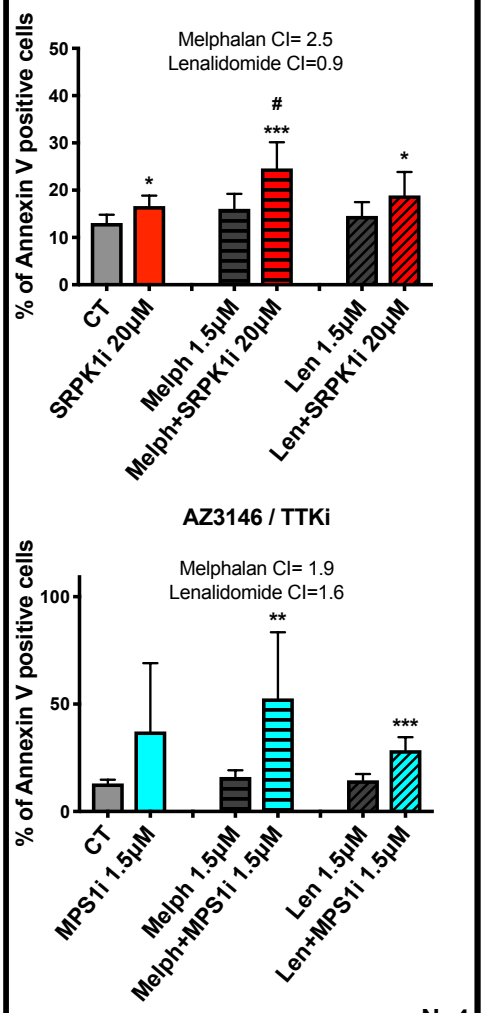


B

Combination Index	Melphalan+CHK1i	Melphalan+MELKi	Melphalan+PLK4i	Melphalan+SRPK1i	Melphalan+CDC7-DBF4i	Melphalan+MPS1i	Melphalan+PBKi
Amo1	0.7	1.1	1.5	2.5	0.7	1.9	1.0
OPM2	0.8	0.8	0.8	1.6	0.5	1.6	0.8
XG1	1.0	1.1	1.2	1.6	0.5	1.8	1.2
XG21	1.1	1.3	0.9	1.4	0.7	1.6	1.1

Combination Index	Lenalidomide+CHK1i	Lenalidomide+MELKi	Lenalidomide+PLK4i	Lenalidomide+SRPK1i	Lenalidomide+CDC7-DBF4i	Lenalidomide+MPS1i	Lenalidomide+PBKi
Amo1	0.6	0.7	1.1	0.9	1.5	1.6	0.8
OPM2	0.8	0.9	0.6	0.7	0.9	1.0	0.7
XG1	1.7	1.6	1.0	1.6	0.5	1.7	1.6
XG21	1.7	1.4	1.1	1.6	1.5	1.5	1.8

C



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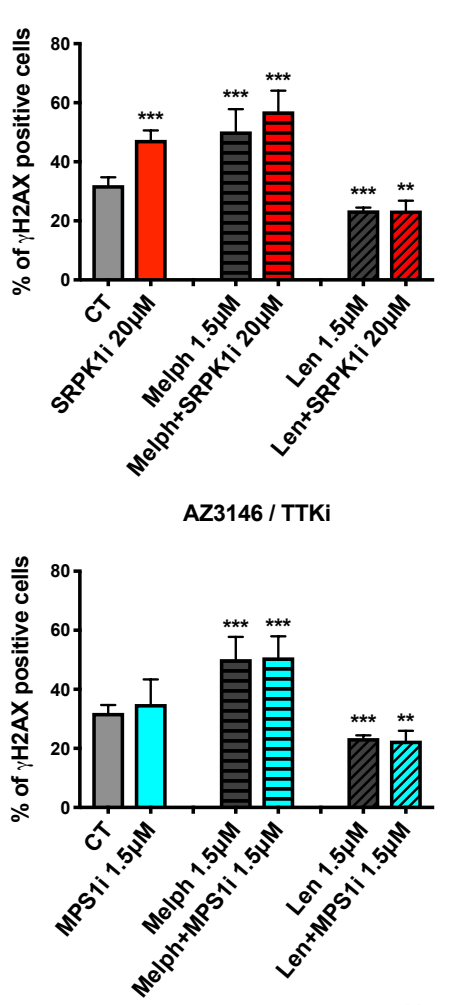

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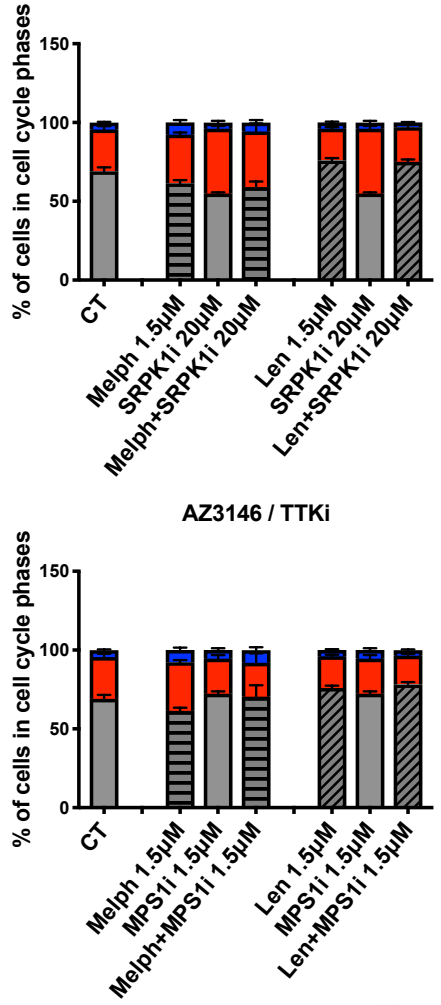
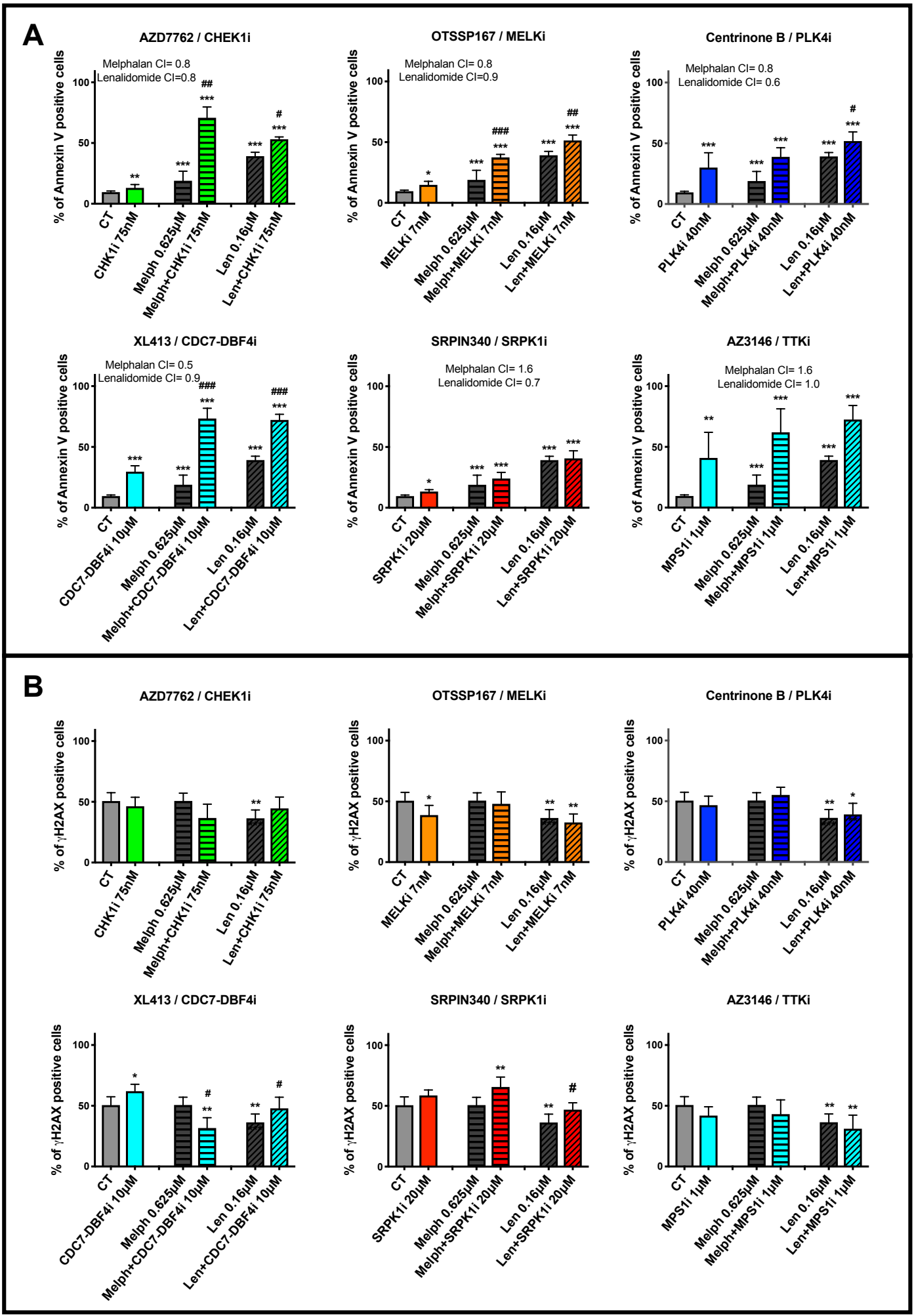
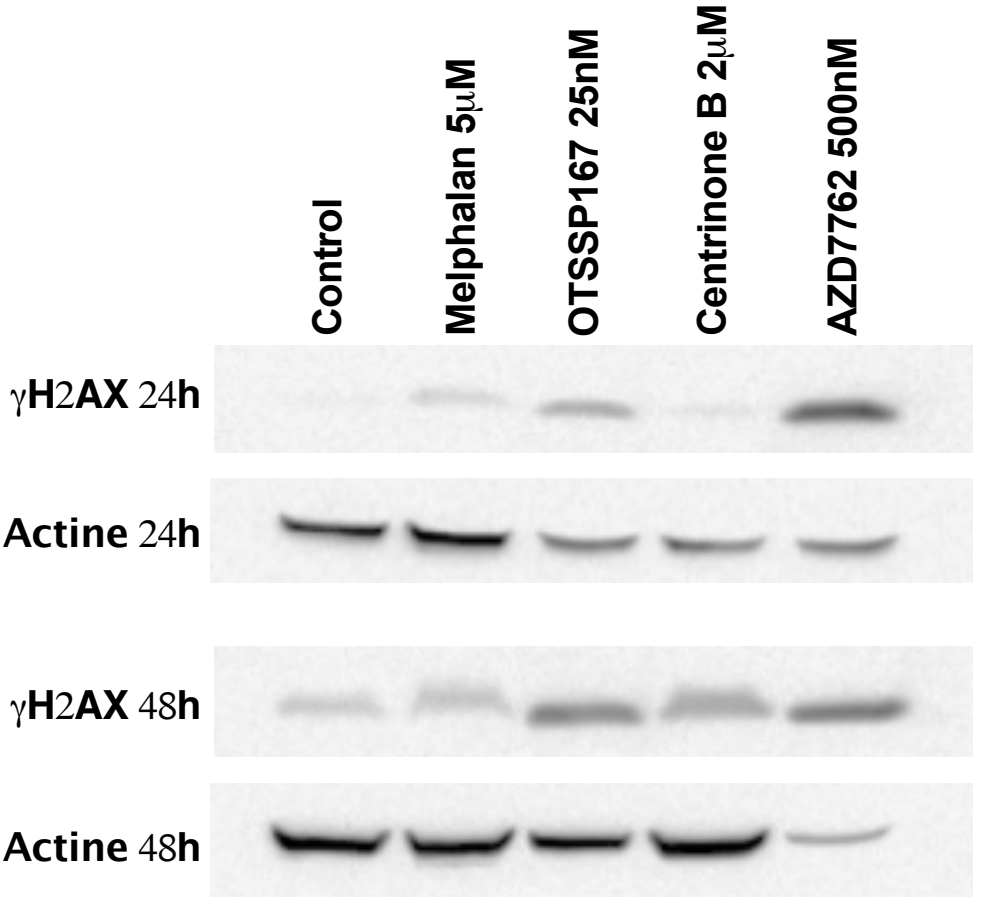


Supplementary Figure 10 OPM2 cell line



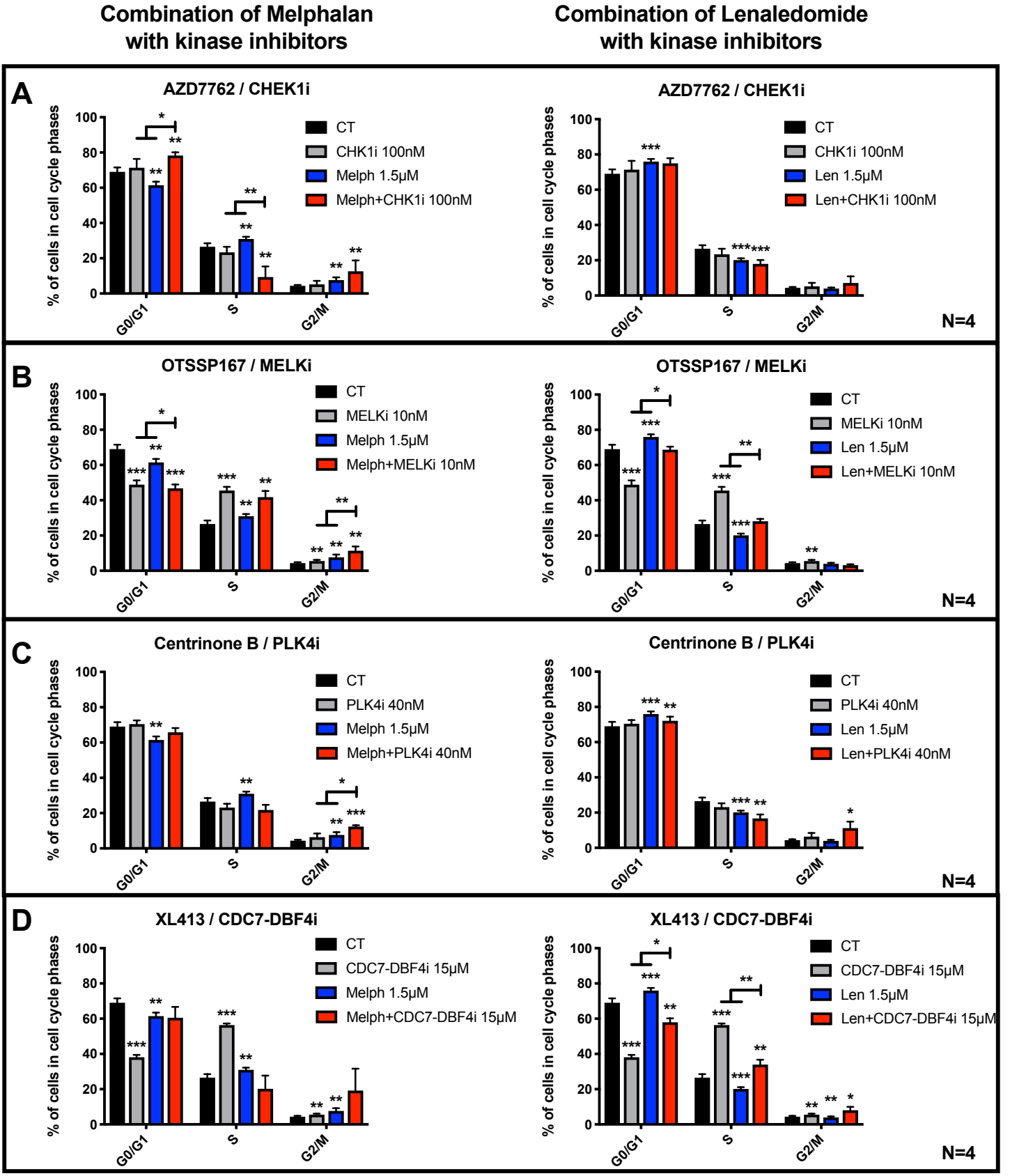
Supplementary Figure 11

γH2AX and Actine Immunoblot of AMO1 proteins after 24h or 48h treatement with Kinases inhibitors.



Supplementary Figure 12

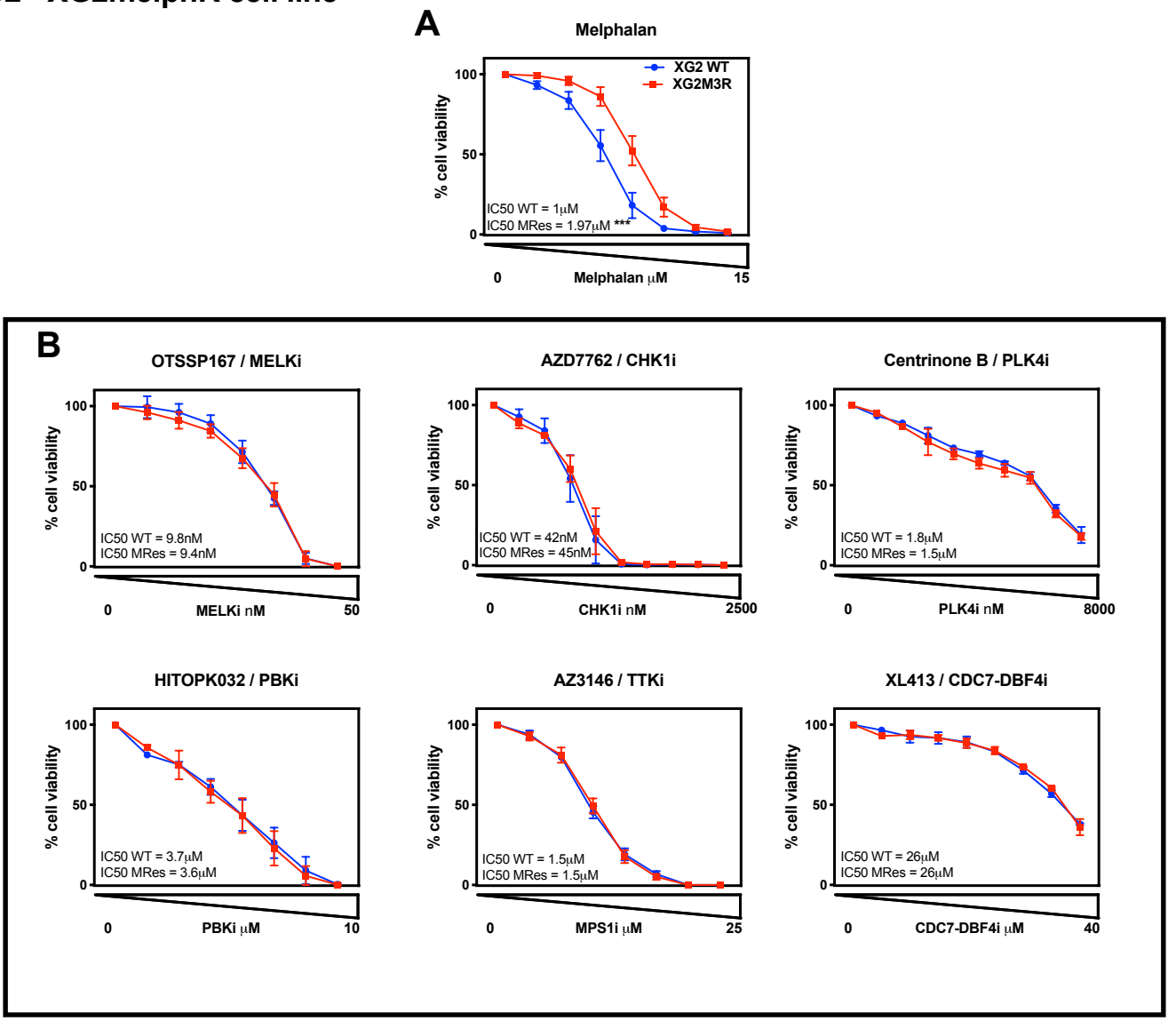
pvalue: *<0.05; **<0.01; ***<0.001



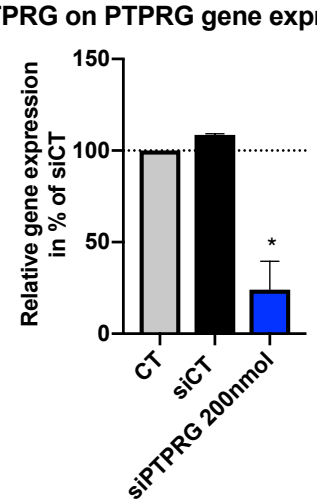
Supplementary Figure 13

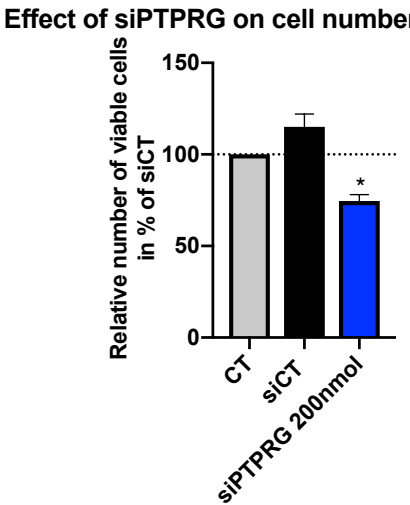
XG2 - XG2melphR cell line

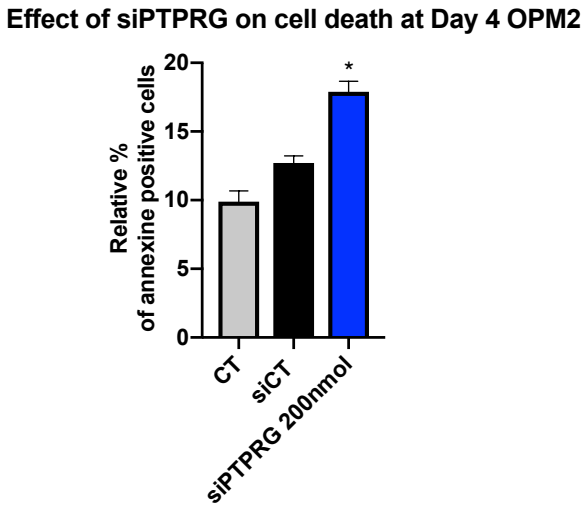
pvalue: *<0.05; **<0.01; ***<0.001



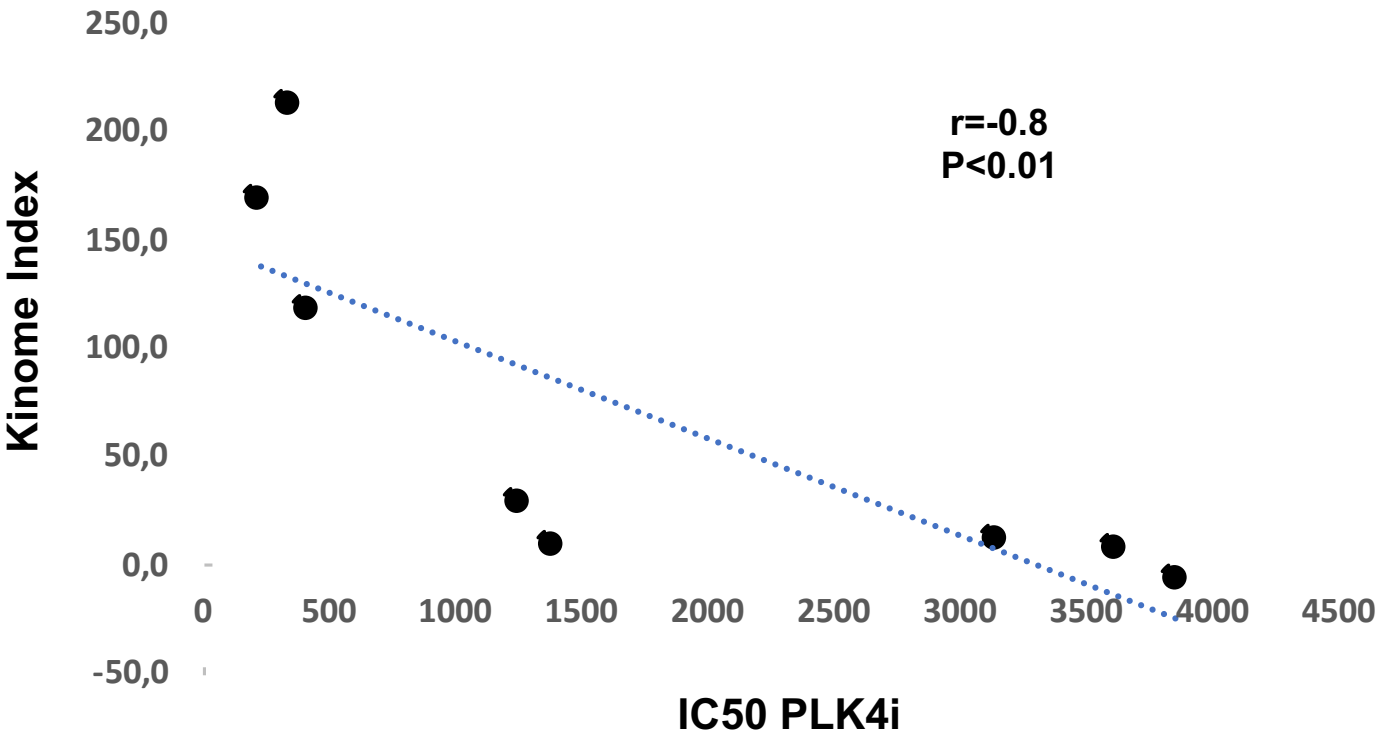
Supplementary Figure 14 OPM2 cell line siPTPRG







Supplementary Figure 15



Supplementary Table S1: list of kinases related probesets (from Sabatier R. et al. Kinome expression profiling and prognosis of basal breast cancers. Mol. Cancer 10, 86 (2011). Reference 10)

AFFYM-PROBESET	GENE	TITLE	CYTOBAND	ENTREZ	REFSEQ ACCESSION NUMBER
212609_s_at	AKT3	v-akt murine thymoma viral oncogene homolog 3 (protein ki	1q43-q44	10000	U79271
209027_s_at	ABI1	abl-interactor 1	10p11.2	10006	BF673013
205042_at	GNE	glucosamine (UDP-N-acetyl)-2-epimerase/N-acetylmannosa	9p13.3	10020	NM_005476
223465_at	COL4A3BP	collagen, type IV, alpha 3 (Goodpasture antigen) binding pro	5q13.3	10087	BE967275
220357_s_at	SGK2	serum/glucocorticoid regulated kinase 2	20q13.2	10110	NM_016276
210148_at	HIPK3	homeodomain interacting protein kinase 3	11p13	10114	AF305239
202207_at	ARL4C	ADP-ribosylation factor-like 4C	2q37.1	10123	BG435404
204252_at	CDK2	cyclin-dependent kinase 2	12q13	1017	M68520
229468_at	CDK3	cyclin-dependent kinase 3	17q22-qter	1018	AI885421
203839_s_at	TNK2	tyrosine kinase, non-receptor, 2	3q29	10188	NM_005781
202246_s_at	CDK4	cyclin-dependent kinase 4	12q14	1019	NM_000075
204247_s_at	CDK5	cyclin-dependent kinase 5	7q36	1020	NM_004935
205851_at	NME6	non-metastatic cells 6, protein expressed in (nucleoside-diph	3p21	10201	BC001808
224851_at	CDK6	cyclin-dependent kinase 6	7q21-q22	1021	AW274756
211297_s_at	CDK7	cyclin-dependent kinase 7	5q12.1	1022	L20320
202241_at	TRIB1	tribbles homolog 1 (Drosophila)	8q24.13	10221	NM_025195
1553112_s_at	CDK8	cyclin-dependent kinase 8	13q12	1024	NM_001260
203198_at	CDK9	cyclin-dependent kinase 9	9q34.1	1025	NM_001261
204740_at	CNKSR1	connector enhancer of kinase suppressor of Ras 1	1p36.11	10256	NM_006314
202284_s_at	CDKN1A	cyclin-dependent kinase inhibitor 1A (p21, Cip1)	6p21.2	1026	NM_000389
209112_at	CDKN1B	cyclin-dependent kinase inhibitor 1B (p27, Kip1)	12p13.1-p12	1027	BC001971
203847_s_at	AKAP8	A kinase (PRKA) anchor protein 8	19p13.1	10270	AW341501
213348_at	CDKN1C	cyclin-dependent kinase inhibitor 1C (p57, Kip2)	11p15.5	1028	N33167
232153_at	SPEG	SPEG complex locus	2q35	10290	AL512705
202030_at	BCKDK	branched chain ketoacid dehydrogenase kinase	16p11.2	10295	NM_005881
33814_at	PAK4	p21 protein (Cdc42/Rac)-activated kinase 4	19q13.2	10298	AF005046
236313_at	CDKN2B	cyclin-dependent kinase inhibitor 2B (p15, inhibits CDK4)	9p21	1030	AW444761
204159_at	CDKN2C	cyclin-dependent kinase inhibitor 2C (p18, inhibits CDK4)	1p32	1031	NM_001262
210240_s_at	CDKN2D	cyclin-dependent kinase inhibitor 2D (p19, inhibits CDK4)	19p13	1032	U20498
1555758_a_at	CDKN3	cyclin-dependent kinase inhibitor 3	14q22	1033	AF213040
205486_at	TESK2	testis-specific kinase 2	1p32	10420	NM_007170
211913_s_at	MERTK	c-mer proto-oncogene tyrosine kinase	2q14.1	10461	L08961
201314_at	STK25	serine/threonine kinase 25 (STE20 homolog, yeast)	2q37.3	10494	NM_006374
211681_s_at	PDLIM5	PDZ and LIM domain 5	4q22	10611	AF116705
213812_s_at	CAMKK2	calcium/calmodulin-dependent protein kinase kinase 2, beta	12q24.2	10645	AK024748
203515_s_at	PMVK	phosphomevalonate kinase	1q22	10654	NM_006556
204887_s_at	PLK4	polo-like kinase 4 (Drosophila)	4q28	10733	NM_014264

221695_s_at	MAP3K2	mitogen-activated protein kinase kinase kinase 2	2q14.3	10746	AF239798
201939_at	PLK2	polo-like kinase 2 (Drosophila)	5q12.1-q13.2	10769	NM_006622
223159_s_at	NEK6	NIMA (never in mitosis gene a)-related kinase 6	9q33.3-q34.11	10783	BC000101
208309_s_at	MALT1	mucosa associated lymphoid tissue lymphoma translocation	18q21	10892	NM_006785
210975_x_at	FASTK	Fas-activated serine/threonine kinase	7q35	10922	BC000377
204244_s_at	DBF4	DBF4 homolog (S. cerevisiae)	7q21.3	10926	NM_006716
212426_s_at	YWHAQ	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase ac	2p25.1	10971	BF033313
212986_s_at	TLK2	tousled-like kinase 2	17q23	11011	BF112255
228139_at	RIPK3	receptor-interacting serine-threonine kinase 3	14q11.2	11035	NM_006871
204269_at	PIM2	pim-2 oncogene	Xp11.23	11040	NM_006875
205651_x_at	RAPGEF4	Rap guanine nucleotide exchange factor (GEF) 4	2q31-q32	11069	NM_007023
205394_at	CHEK1	CHK1 checkpoint homolog (S. pombe)	11q24-q24	1111	NM_001274
212801_at	CIT	citron (rho-interacting, serine/threonine kinase 21)	12q24	11113	AI861788
205948_at	PTPRT	protein tyrosine phosphatase, receptor type, T	20q12-q13	11122	NM_007050
203553_s_at	MAP4K5	mitogen-activated protein kinase kinase kinase kinase 5	14q11.2-q21	11183	NM_006575
214339_s_at	MAP4K1	mitogen-activated protein kinase kinase kinase kinase 1	19q13.1-q13.4	11184	AA744529
204233_s_at	CHKA	choline kinase alpha	11q13.2	1119	AI991328
204712_at	WIF1	WNT inhibitory factor 1	12q14.3	11197	NM_007191
210069_at	CHKB	choline kinase beta	22q13.33	1120	U62733
210416_s_at	CHEK2	CHK2 checkpoint homolog (S. pombe)	22q11|22q12.	11200	BC004207
220034_at	IRAK3	interleukin-1 receptor-associated kinase 3	12q14.3	11213	NM_007199
227039_at	AKAP13	A kinase (PRKA) anchor protein 13	15q24-q25	11214	AI674926
215336_at	AKAP11	A kinase (PRKA) anchor protein 11	13q14.11	11215	AK002166
221563_at	DUSP10	dual specificity phosphatase 10	1q41	11221	N36770
218961_s_at	PNKP	polynucleotide kinase 3'-phosphatase	19q13.3-q13.4	11284	NM_007254
225402_at	TP53RK	TP53 regulating kinase	20q13.2	112858	BG339450
1557145_at	STK38	serine/threonine kinase 38	6p21	11329	BU617137
202009_at	TWF2	twinfilin, actin-binding protein, homolog 2 (Drosophila)	3p21.1	11344	NM_007284
209666_s_at	CHUK	conserved helix-loop-helix ubiquitous kinase	10q24-q25	1147	AF080157
1557103_a_at	LMTK3	lemur tyrosine kinase 3	19q13.32	114783	BE868592
200884_at	CKB	creatine kinase, brain	14q32	1152	NM_001823
228367_at	ALPK2	alpha-kinase 2	8q21.31-q21.3	115701	BE551416
226411_at	EVI5L	ecotropic viral integration site 5-like	19p13.2	115704	N32544
204810_s_at	CKM	creatine kinase, muscle	19q13.2-q13.3	1158	NM_001824
202712_s_at	CKMT1B	creatine kinase, mitochondrial 1B	15q15	1159	NM_020990
205295_at	CKMT2	creatine kinase, mitochondrial 2 (sarcomeric)	5q13.3	1160	NM_001825
201897_s_at	CKS1B	CDC28 protein kinase regulatory subunit 1B	1q21.2	1163	NM_001826
204170_s_at	CKS2	CDC28 protein kinase regulatory subunit 2	9q22	1164	NM_001827
231179_at	IHPK3	inositol hexaphosphate kinase 3	6p21.31	117283	R99291
214683_s_at	CLK1	CDC-like kinase 1	2q33	1195	AI251890

203229_s_at	CLK2	CDC-like kinase 2	1q21	1196	NM_003993
202140_s_at	CLK3	CDC-like kinase 3	15q24	1198	NM_003992
1553292_s_at	FLJ25006	uncharacterized serine/threonine-protein kinase SgK494	17q11.2	124923	NM_144610
235003_at	UHMK1	U2AF homology motif (UHM) kinase 1	1q23.3	127933	AI249980
1552519_at	ACVR1C	activin A receptor, type IC	2q24.1	130399	NM_145259
228399_at	OSR1	odd-skipped related 1 (Drosophila)	2p24.1	130497	AI569974
204119_s_at	ADK	adenosine kinase	q22|10q11-q	132	U90339
235421_at	MAP3K8	mitogen-activated protein kinase kinase kinase 8	10p11.23	1326	AV713062
206184_at	CRKL	v-crk sarcoma virus CT10 oncogene homolog (avian)-like	2q11|22q11.2	1399	NM_005207
1552578_a_at	MYO3B	myosin IIIB	2q31.1-q31.2	140469	NM_138995
212530_at	NEK7	NIMA (never in mitosis gene a)-related kinase 7	1q31.3	140609	AL080111
224412_s_at	TRPM6	transient receptor potential cation channel, subfamily M, me	9q21.13	140803	AF350881
225649_s_at	STK35	serine/threonine kinase 35	20p13	140901	AA001414
202530_at	MAPK14	mitogen-activated protein kinase 14	6p21.3-p21.2	1432	NM_001315
203104_at	CSF1R	colony stimulating factor 1 receptor	5q33-q35	1436	NM_005211
202329_at	CSK	c-src tyrosine kinase	15q23-q25	1445	NM_004383
243338_at	CSNK1A1	casein kinase 1, alpha 1	5q32	1452	AI674461
207945_s_at	CSNK1D	casein kinase 1, delta	17q25	1453	NM_001893
226858_at	CSNK1E	casein kinase 1, epsilon	22q13.1	1454	T51255
202574_s_at	CSNK1G2	casein kinase 1, gamma 2	19p13.3	1455	NM_001319
227767_at	CSNK1G3	casein kinase 1, gamma 3	5q23	1456	AI073822
212075_s_at	CSNK2A1	casein kinase 2, alpha 1 polypeptide	20p13	1457	AI161318
224922_at	CSNK2A2	casein kinase 2, alpha prime polypeptide	16q21	1459	AI022089
231777_at	CSNK2B	casein kinase 2, beta polypeptide	21-p12|6p21	1460	NM_021221
1557073_s_at	TTBK2	tau tubulin kinase 2	15q15.2	146057	AK074481
235642_at	ADRA1A	adrenergic, alpha-1A-, receptor	8p21-p11.2	148	AV694854
227255_at	PDIK1L	PDLIM1 interacting kinase 1 like	1p36.11	149420	AI806633
208078_s_at	SNF1LK	SNF1-like kinase	21q22.3	150094	NM_030751
206170_at	ADRB2	adrenergic, beta-2-, receptor, surface	5q31-q32	154	NM_000024
201401_s_at	ADRBK1	adrenergic, beta, receptor kinase 1	11q13.1	156	M80776
228771_at	ADRBK2	adrenergic, beta, receptor kinase 2	2q11|22q12.	157	AI651212
235085_at	PRAGMIN	homolog of rat pragma of Rnd2	8p23.1	157285	BF739767
211272_s_at	DGKA	diacylglycerol kinase, alpha 80kDa	12q13.3	1606	AF064771
226605_at	DGKQ	diacylglycerol kinase, theta 110kDa	4p16.3	1609	N45308
203139_at	DAPK1	death-associated protein kinase 1	9q34.1	1612	NM_004938
203890_s_at	DAPK3	death-associated protein kinase 3	19p13.3	1613	BF686824
203302_at	DCK	deoxycytidine kinase	4q13.3-q21.1	1633	NM_000788
227666_at	DCLK2	doublecortin-like kinase 2	4q31.3	166614	AI523594
230864_at	MGC42105	serine/threonine-protein kinase NIM1	5p12	167359	BF222940
203816_at	DGUOK	deoxyguanosine kinase	2p13	1716	NM_001929

202516_s_at	DLG1	discs, large homolog 1 (Drosophila)	3q29	1739	NM_004087
212729_at	DLG3	discs, large homolog 3 (neuroendocrine-dlg, Drosophila)	Xq13.1	1741	AI916274
210684_s_at	DLG4	discs, large homolog 4 (Drosophila)	17p13.1	1742	AF028825
37996_s_at	DMPK	dystrophia myotonica-protein kinase	19q13.3	1760	L08835
216835_s_at	DOK1	docking protein 1, 62kDa (downstream of tyrosine kinase 1)	2p13	1796	AF035299
203270_at	DTYMK	deoxythymidylate kinase (thymidylate kinase)	2q37.3	1841	NM_012145
201041_s_at	DUSP1	dual specificity phosphatase 1	5q34	1843	NM_004417
204794_at	DUSP2	dual specificity phosphatase 2	2q11	1844	NM_004418
204014_at	DUSP4	dual specificity phosphatase 4	8p12-p11	1846	NM_001394
209457_at	DUSP5	dual specificity phosphatase 5	10q25	1847	U16996
208892_s_at	DUSP6	dual specificity phosphatase 6	12q22-q23	1848	BC003143
206374_at	DUSP8	dual specificity phosphatase 8	11p15.5	1850	NM_004420
209033_s_at	DYRK1A	dual-specificity tyrosine-(Y)-phosphorylation regulated kinas	21q22.13	1859	D86550
206758_at	EDN2	endothelin 2	1p34	1907	NM_001956
201983_s_at	EGFR	epidermal growth factor receptor (erythroblastic leukemia vi	7p12	1956	AW157070
203499_at	EPHA2	EPH receptor A2	1p36	1969	NM_004431
226072_at	FUK	fucokinase	16q22.1	197258	AW080798
238025_at	MLKL	mixed lineage kinase domain-like	16q22.3	197259	AA706818
203942_s_at	MARK2	MAP/microtubule affinity-regulating kinase 2	11q12-q13	2011	NM_017490
202587_s_at	AK1	adenylate kinase 1	9q34.1	203	BC001116
228524_at	ADCK5	aarF domain containing kinase 5	8q24.3	203054	BE856488
212172_at	AK2	adenylate kinase 2	1p34	204	AW277253
205977_s_at	EPHA1	EPH receptor A1	7q34	2041	NM_005232
206070_s_at	EPHA3	EPH receptor A3	3p11.2	2042	AF213459
228948_at	EPHA4	EPH receptor A4	2q36.1	2043	T15545
238533_at	EPHA7	EPH receptor A7	6q16.1	2045	AA651750
1554069_at	EPHA8	EPH receptor A8	1p36.12	2046	BC038796
230425_at	EPHB1	EPH receptor B1	3q21-q23	2047	AI674183
209589_s_at	EPHB2	EPH receptor B2	1p36.1-p35	2048	AF025304
1552516_a_at	HIPK1	homeodomain interacting protein kinase 1	1p13.2	204851	NM_152696
1438_at	EPHB3	EPH receptor B3	3q21-qter	2049	X75208
225342_at	AK3L1	adenylate kinase 3-like 1	1p31.3	205	AK026966
202894_at	EPHB4	EPH receptor B4	7q22	2050	NM_004444
204718_at	EPHB6	EPH receptor B6	7q33-q35	2051	NM_004445
216836_s_at	ERBB2	v-erb-b2 erythroblastic leukemia viral oncogene homolog 2,	1.2-q12|17q	2064	X03363
202454_s_at	ERBB3	v-erb-b2 erythroblastic leukemia viral oncogene homolog 3 (	12q13	2065	NM_001982
214053_at	ERBB4	v-erb-a erythroblastic leukemia viral oncogene homolog 4 (a	2q33.3-q34	2066	AW772192
207163_s_at	AKT1	v-akt murine thymoma viral oncogene homolog 1	32.32|14q32	207	NM_005163
211453_s_at	AKT2	v-akt murine thymoma viral oncogene homolog 2	9q13.1-q13.2	208	M77198
235745_at	ERN1	endoplasmic reticulum to nucleus signaling 1	17q24.2	2081	AV704183

221884_at	EVI1	ecotropic viral integration site 1	3q24-q28	2122	BE466525
203110_at	PTK2B	PTK2B protein tyrosine kinase 2 beta	8p21.1	2185	U43522
1564002_a_at	AKD1	adenylate kinase domain containing 1	6q21	221264	AK092103
206412_at	FER	fer (fps/fes related) tyrosine kinase	5q21	2241	NM_005246
205418_at	FES	feline sarcoma oncogene	15q26.1	2242	NM_002005
222164_at	FGFR1	fibroblast growth factor receptor 1	8p11.2-p11.1	2260	AU145411
208228_s_at	FGFR2	fibroblast growth factor receptor 2	10q26	2263	M87771
204579_at	FGFR4	fibroblast growth factor receptor 4	5q35.1-qter	2264	NM_002011
208438_s_at	FGR	Gardner-Rasheed feline sarcoma viral (v-fgr) oncogene hom	1p36.2-p36.1	2268	NM_005248
205434_s_at	AAK1	AP2 associated kinase 1	2p14	22848	AW451954
204569_at	ICK	intestinal cell (MAK-like) kinase	6p12.1	22858	NM_014920
208941_s_at	SEPHS1	selenophosphate synthetase 1	10p14	22929	BC000941
212572_at	STK38L	serine/threonine kinase 38 like	12p11.23	23012	AW779556
213045_at	MAST3	microtubule associated serine/threonine kinase 3	19p13.11	23031	AB011133
213107_at	TNIK	TRAF2 and NCK interacting kinase	3q26.2-q26.31	23043	R59093
210057_at	SMG1	PI-3-kinase-related kinase SMG-1	16p12.3	23049	U32581
215660_s_at	MAST2	microtubule associated serine/threonine kinase 2	1p34.1	23139	AK025352
213178_s_at	MAPK8IP3	mitogen-activated protein kinase 8 interacting protein 3	16p13.3	23162	AB028989
213534_s_at	PASK	PAS domain containing serine/threonine kinase	2q37.3	23178	D50925
222033_s_at	FLT1	fms-related tyrosine kinase 1 (vascular endothelial growth fa	13q12	2321	AA058828
206674_at	FLT3	fms-related tyrosine kinase 3	13q12	2322	NM_004119
223430_at	SNF1LK2	SNF1-like kinase 2	11q23.1	23235	AL136764
229902_at	FLT4	fms-related tyrosine kinase 4	5q35.3	2324	AW083785
202962_at	KIF13B	kinesin family member 13B	8p21.1	23303	NM_015254
204156_at	KIAA0999	KIAA0999 protein	11q23.3	23387	AA044154
205050_s_at	MAPK8IP2	mitogen-activated protein kinase 8 interacting protein 2	22q13.33	23542	NM_012324
205271_s_at	CCRK	cell cycle related kinase	9q22.1	23552	NM_012119
215184_at	DAPK2	death-associated protein kinase 2	15q22.31	23604	AK026801
220038_at	SGK3	serum/glucocorticoid regulated kinase family, member 3	8q12.3-q13.1	23678	NM_013257
218236_s_at	PRKD3	protein kinase D3	2p21	23683	NM_005813
219713_at	SHPK	sedoheptulokinase	17p13	23729	NM_013276
208212_s_at	ALK	anaplastic lymphoma receptor tyrosine kinase	2p23	238	NM_004304
205565_s_at	FXN	frataxin	9q13-q21.1	2395	NM_000144
202288_at	FRAP1	FK506 binding protein 12-rapamycin associated protein 1	1p36.2	2475	U88966
202123_s_at	ABL1	c-abl oncogene 1, receptor tyrosine kinase	9q34.1	25	NM_005157
227266_s_at	FYB	FYN binding protein (FYB-120/130)	5p13.1	2533	BF679849
212486_s_at	FYN	FYN oncogene related to SRC, FGR, YES	6q21	2534	N20923
40225_at	GAK	cyclin G associated kinase	4p16	2580	D88435
204374_s_at	GALK1	galactokinase 1	17q24	2584	BG474736
205219_s_at	GALK2	galactokinase 2	15q21.1	2585	NM_002044

38269_at	PRKD2	protein kinase D2	19q13.3	25865	AL050147
225067_at	ULK3	unc-51-like kinase 3 (C. elegans)	15q24.1	25989	AL117482
218688_at	DAK	dihydroxyacetone kinase 2 homolog (S. cerevisiae)	11q12.2	26007	NM_015533
226770_at	MAGI3	membrane associated guanylate kinase, WW and PDZ doma	1p12-p11.2	260425	AI692181
222538_s_at	APPL1	adaptor protein, phosphotyrosine interaction, PH domain and	3p21.1-p14.3	26060	AW467472
222862_s_at	AK5	adenylate kinase 5	1p31	26289	BG169832
221667_s_at	HSPB8	heat shock 22kDa protein 8	12q24.23	26353	AF133207
223380_s_at	LATS2	LATS, large tumor suppressor, homolog 2 (Drosophila)	13q11-q12	26524	AF207547
206216_at	SRPK3	SFRS protein kinase 3	Xq28	26576	NM_014370
205721_at	GFRA2	GDNF family receptor alpha 2	8p21.3	2675	U97145
218909_at	RPS6KC1	ribosomal protein S6 kinase, 52kDa, polypeptide 1	1q41	26750	NM_012424
221207_s_at	NBEA	neurobeachin	13q13	26960	NM_015678
231907_at	ABL2	v-abl Abelson murine leukemia viral oncogene homolog 2 (a	1q24-q25	27	AK025877
221218_s_at	TPK1	thiamin pyrophosphokinase 1	7q34-q35	27010	NM_022445
207387_s_at	GK	glycerol kinase	Xp21.3	2710	NM_000167
231806_s_at	STK36	serine/threonine kinase 36, fused homolog (Drosophila)	2q35	27148	AL133630
202786_at	STK39	serine threonine kinase 39 (STE20/SPS1 homolog, yeast)	2q24.3	27347	NM_013233
202543_s_at	GMFB	glia maturation factor, beta	14q22.2	2764	BC005359
230934_at	STK32C	serine/threonine kinase 32C	10q26.3	282974	BF508609
230551_at	KSR2	kinase suppressor of ras 2	2q24.22-q24.2	283455	AI692426
1557170_at	NEK8	NIMA (never in mitosis gene a)- related kinase 8	17q11.1	284086	AI073943
204396_s_at	GRK5	G protein-coupled receptor kinase 5	10q24-qter	2869	NM_005308
211543_s_at	GRK6	G protein-coupled receptor kinase 6	5q35	2870	AF040752
223199_at	MKNK2	MAP kinase interacting serine/threonine kinase 2	19p13.3	2872	AA404592
202478_at	TRIB2	tribbles homolog 2 (Drosophila)	2p25.1-p24.3	28951	NM_021643
225115_at	HIPK2	homeodomain interacting protein kinase 2	7q32-q34	28996	BF529628
218520_at	TBK1	TANK-binding kinase 1	12q14.1	29110	NM_013254
632_at	GSK3A	glycogen synthase kinase 3 alpha	19q13.2	2931	L40027
209945_s_at	GSK3B	glycogen synthase kinase 3 beta	3q13.3	2932	BC000251
202451_at	GTF2H1	general transcription factor IIH, polypeptide 1, 62kDa	11p15.1-p14	2965	BC000365
207655_s_at	BLNK	B-cell linker	0q23.2-q23.3	29760	NM_013314
210026_s_at	CARD10	caspase recruitment domain family, member 10	22q13.1	29775	AY028896
200075_s_at	GUK1	guanylate kinase 1	1q32-q41	2987	BC006249
225546_at	EEF2K	eukaryotic elongation factor-2 kinase	16p12.1	29904	W68180
227556_at	NME7	non-metastatic cells 7, protein expressed in (nucleoside-diph	1q24	29922	AI094580
226299_at	PKN3	protein kinase N3	9q34.11	29941	NM_013355
217765_at	NRBP1	nuclear receptor binding protein 1	2p23	29959	NM_013392
227053_at	PACSIN1	protein kinase C and casein kinase substrate in neurons 1	6p21.3	29993	N47315
208018_s_at	HCK	hemopoietic cell kinase	20q11-q12	3055	NM_002110
1555935_s_at	HUNK	hormonally up-regulated Neu-associated kinase	21q22.1	30811	T58129

212740_at	PIK3R4	phosphoinositide-3-kinase, regulatory subunit 4	3q22.1	30849	BF740111
200697_at	HK1	hexokinase 1	10q22	3098	NM_000188
202934_at	HK2	hexokinase 2	2p13	3099	AI761561
205936_s_at	HK3	hexokinase 3 (white cell)	5q35.2	3101	NM_002115
225949_at	NRBP2	nuclear receptor binding protein 2	8q24.3	340371	N21030
225330_at	IGF1R	insulin-like growth factor 1 receptor	15q26.3	3480	AL044092
239061_at	TPRXL	tetra-peptide repeat homeobox-like	3p25.1	348825	AW303358
209341_s_at	IKBKB	inhibitor of kappa light polypeptide gene enhancer in B-cells,	8p11.2	3551	AU153366
201234_at	ILK	integrin-linked kinase	11p15.5-p15.4	3611	NM_004517
204533_at	CXCL10	chemokine (C-X-C motif) ligand 10	4q21	3627	NM_001565
226216_at	INSR	insulin receptor	19p13.3-p13.2	3643	W84556
201587_s_at	IRAK1	interleukin-1 receptor-associated kinase 1	Xq28	3654	NM_001569
231779_at	IRAK2	interleukin-1 receptor-associated kinase 2	3p25.3	3656	AI246590
204686_at	IRS1	insulin receptor substrate 1	2q36	3667	NM_005544
201895_at	ARAF	v-raf murine sarcoma 3611 viral oncogene homolog	Xp11.4-p11.2	369	NM_001654
211339_s_at	ITK	IL2-inducible T-cell kinase	5q31-q32	3702	D13720
210740_s_at	ITPK1	inositol 1,3,4-triphosphate 5/6 kinase	14q31	3705	AF279372
235213_at	ITPKB	inositol 1,4,5-trisphosphate 3-kinase B	1q42.13	3707	AA348410
239695_at	JAK1	Janus kinase 1 (a protein tyrosine kinase)	1p32.3-p31.3	3716	AI280194
1562031_at	JAK2	Janus kinase 2 (a protein tyrosine kinase)	9p24	3717	BC043187
227677_at	JAK3	Janus kinase 3 (a protein tyrosine kinase, leukocyte)	19p13.1	3718	BF512748
203934_at	KDR	kinase insert domain receptor (a type III receptor tyrosine kir	4q11-q12	3791	NM_002253
211028_s_at	KHK	ketohexokinase (fructokinase)	2p23.3	3795	BC006233
205051_s_at	KIT	v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene hom	4q11-q12	3815	NM_000222
204891_s_at	LCK	lymphocyte-specific protein tyrosine kinase	1p34.3	3932	NM_005356
205269_at	LCP2	lymphocyte cytosolic protein 2 (SH2 domain containing leukc	5q33.1-qter	3937	AI123251
204357_s_at	LIMK1	LIM domain kinase 1	7q11.23	3984	NM_002314
217475_s_at	LIMK2	LIM domain kinase 2	22q12.2	3985	AC002073
207106_s_at	LTK	leukocyte receptor tyrosine kinase	15q15.1-q21.1	4058	NM_002344
202626_s_at	LYN	v-yes-1 Yamaguchi sarcoma viral related oncogene homolog	8q13	4067	NM_002350
207069_s_at	SMAD6	SMAD family member 6	15q21-q22	4091	NM_005585
220302_at	MAK	male germ cell-associated kinase	6p24	4117	NM_005906
226653_at	MARK1	MAP/microtubule affinity-regulating kinase 1	1q41	4139	AB040910
202569_s_at	MARK3	MAP/microtubule affinity-regulating kinase 3	14q32.3	4140	NM_002376
206267_s_at	MATK	megakaryocyte-associated tyrosine kinase	19p13.3	4145	NM_002378
214786_at	MAP3K1	mitogen-activated protein kinase kinase kinase 1	5q11.2	4214	AA361361
203514_at	MAP3K3	mitogen-activated protein kinase kinase kinase 3	17q23.3	4215	BF971923
216199_s_at	MAP3K4	mitogen-activated protein kinase kinase kinase 4	6q26	4216	AL109942
203836_s_at	MAP3K5	mitogen-activated protein kinase kinase kinase 5	6q22.33	4217	D84476
203510_at	MET	met proto-oncogene (hepatocyte growth factor receptor)	7q31	4233	BG170541

213927_at	MAP3K9	mitogen-activated protein kinase kinase kinase 9	14q24.3-q31	4293	AV753204
206362_x_at	MAP3K10	mitogen-activated protein kinase kinase kinase 10	19q13.2	4294	NM_002446
203652_at	MAP3K11	mitogen-activated protein kinase kinase kinase 11	l1q13.1-q13.3	4296	NM_002419
202974_at	MPP1	membrane protein, palmitoylated 1, 55kDa	Xq28	4354	NM_002436
207984_s_at	MPP2	membrane protein, palmitoylated 2 (MAGUK p55 subfamily	17q12-q21	4355	NM_005374
206186_at	MPP3	membrane protein, palmitoylated 3 (MAGUK p55 subfamily	17q21.31	4356	NM_001932
225164_s_at	EIF2AK4	eukaryotic translation initiation factor 2 alpha kinase 4	15q15.1	440275	AB037759
205455_at	MST1R	macrophage stimulating 1 receptor (c-met-related tyrosine l	3p21.3	4486	NM_002447
203027_s_at	MVD	mevalonate (diphospho) decarboxylase	16q24.3	4597	AI189359
215649_s_at	MVK	mevalonate kinase	12q24	4598	AF217536
224823_at	MYLK	myosin light chain kinase	3q21	4638	AA526844
203978_at	NUBP1	nucleotide binding protein 1 (MinD homolog, E. coli)	16p13.13	4682	NM_002484
208442_s_at	ATM	ataxia telangiectasia mutated	11q22-q23	472	NM_000051
213328_at	NEK1	NIMA (never in mitosis gene a)-related kinase 1	4q33	4750	AI936517
204641_at	NEK2	NIMA (never in mitosis gene a)-related kinase 2	1q32.2-q41	4751	NM_002497
213116_at	NEK3	NIMA (never in mitosis gene a)-related kinase 3	13q14.13	4752	AI191920
201577_at	NME1	non-metastatic cells 1, protein (NM23A) expressed in	17q21.3	4830	NM_000269
201268_at	NME2	non-metastatic cells 2, protein (NM23B) expressed in	17q21.3	4831	NM_002512
204862_s_at	NME3	non-metastatic cells 3, protein expressed in	16q13	4832	NM_002513
212739_s_at	NME4	non-metastatic cells 4, protein expressed in	16p13.3	4833	AL523860
32625_at	NPR1	natriuretic peptide receptor A/guanylate cyclase A (atrionatr	1q21-q22	4881	X15357
204310_s_at	NPR2	natriuretic peptide receptor B/guanylate cyclase B (atrionatr	9p21-p12	4882	NM_003995
221796_at	NTRK2	neurotrophic tyrosine kinase, receptor, type 2	9q22.1	4915	AA707199
215025_at	NTRK3	neurotrophic tyrosine kinase, receptor, type 3	15q25	4916	S76476
205805_s_at	ROR1	receptor tyrosine kinase-like orphan receptor 1	1p32-p31	4919	NM_005012
205578_at	ROR2	receptor tyrosine kinase-like orphan receptor 2	9q22	4920	NM_004560
227561_at	DDR2	discoidin domain receptor tyrosine kinase 2	1q23.3	4921	W73819
214625_s_at	MINK1	misshapen-like kinase 1 (zebrafish)	17p13.2	50488	AF218033
208680_at	PRDX1	peroxiredoxin 1	1p34.1	5052	L19184
209615_s_at	PAK1	p21 protein (Cdc42/Rac)-activated kinase 1	11q13-q14	5058	U51120
1559052_s_at	PAK2	p21 protein (Cdc42/Rac)-activated kinase 2	3q29	5062	U25975
214607_at	PAK3	p21 protein (Cdc42/Rac)-activated kinase 3	Xq22.3	5063	AW085556
224151_s_at	AK3	adenylate kinase 3	9p24.1-p24.3	50808	AF183419
217147_s_at	TRAT1	T cell receptor associated transmembrane adaptor 1	3q13	50852	AJ240085
208383_s_at	PCK1	phosphoenolpyruvate carboxykinase 1 (soluble)	20q13.31	5105	NM_002591
202847_at	PCK2	phosphoenolpyruvate carboxykinase 2 (mitochondrial)	14q12	5106	NM_004563
221998_s_at	VRK3	vaccinia related kinase 3	19q13	51231	BF062886
1561190_at	CDKL3	cyclin-dependent kinase-like 3	5q31	51265	AF087989
207239_s_at	PCTK1	PCTAIRE protein kinase 1	(p11.3-p11.23	5127	NM_006201
221918_at	PCTK2	PCTAIRE protein kinase 2	12q23.1	5128	AI742210

214797_s_at	PCTK3	PCTAIRE protein kinase 3	1q31-q32	5129	BC000281
221508_at	TAOK3	TAO kinase 3	12q	51347	AF181985
223165_s_at	IHPK2	inositol hexaphosphate kinase 2	3p21.31	51447	BC004469
203131_at	PDGFRA	platelet-derived growth factor receptor, alpha polypeptide	4q11-q13	5156	NM_006206
218411_s_at	MBIP	MAP3K12 binding inhibitory protein 1	14q13.3	51562	NM_016586
202273_at	PDGFRB	platelet-derived growth factor receptor, beta polypeptide	5q31-q32	5159	NM_002609
226452_at	PDK1	pyruvate dehydrogenase kinase, isozyme 1	2q31.1	5163	AU146532
202590_s_at	PDK2	pyruvate dehydrogenase kinase, isozyme 2	17q21.33	5164	AL574319
206348_s_at	PDK3	pyruvate dehydrogenase kinase, isozyme 3	Xp22.11	5165	NM_005391
218315_s_at	CDK5RAP1	CDK5 regulatory subunit associated protein 1	20pter-q11.23	51654	NM_016408
225207_at	PDK4	pyruvate dehydrogenase kinase, isozyme 4	7q21.3	5166	AV707102
204524_at	PDPK1	3-phosphoinositide dependent protein kinase-1	16p13.3	5170	NM_002613
218318_s_at	NLK	nemo-like kinase	17q11.2	51701	NM_016231
217870_s_at	CMPK1	cytidine monophosphate (UMP-CMP) kinase 1, cytosolic	1p32	51727	NM_016308
213557_at	CRKRS	Cdc2-related kinase, arginine/serine-rich	17q12	51755	AW305119
218499_at	RP6-213H19.1	serine/threonine protein kinase MST4	Xq26.2	51765	NM_016542
223519_at	ZAK	sterile alpha motif and leucine zipper containing kinase AZK	2q24.2	51776	AW069181
207537_at	PFKFB1	6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 1	Xp11.21	5207	NM_002625
226733_at	PFKFB2	6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 2	1q31	5208	AA587884
202464_s_at	PFKFB3	6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 3	10p14-p15	5209	NM_004566
228499_at	PFKFB4	6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 4	3p22-p21	5210	AL038787
201102_s_at	PFKL	phosphofructokinase, liver	21q22.3	5211	NM_002626
210976_s_at	PFKM	phosphofructokinase, muscle	12q13.3	5213	U24183
201037_at	PFKP	phosphofructokinase, platelet	10p15.3-p15.2	5214	NM_002627
204604_at	PFTK1	PFTAIRE protein kinase 1	7q21-q22	5218	NM_012395
217356_s_at	PGK1	phosphoglycerate kinase 1	Xq13	5230	S81916
229876_at	PHKA1	phosphorylase kinase, alpha 1 (muscle)	Xq12-q13	5255	BE503584
209439_s_at	PHKA2	phosphorylase kinase, alpha 2 (liver)	Xp22.2-p22.1	5256	D38616
207312_at	PHKG1	phosphorylase kinase, gamma 1 (muscle)	7p11.2	5260	NM_006213
203709_at	PHKG2	phosphorylase kinase, gamma 2 (testis)	16p12.1-p11.2	5261	NM_000294
1553694_a_at	PIK3C2A	phosphoinositide-3-kinase, class 2, alpha polypeptide	11p15.5-p14	5286	NM_002645
204484_at	PIK3C2B	phosphoinositide-3-kinase, class 2, beta polypeptide	1q32	5287	NM_002646
215129_at	PIK3C2G	phosphoinositide-3-kinase, class 2, gamma polypeptide	12p12	5288	AJ000008
204369_at	PIK3CA	phosphoinositide-3-kinase, catalytic, alpha polypeptide	3q26.3	5290	NM_006218
217620_s_at	PIK3CB	phosphoinositide-3-kinase, catalytic, beta polypeptide	3q22.3	5291	AA805318
209193_at	PIM1	pim-1 oncogene	6p21.2	5292	M24779
1568629_s_at	PIK3R2	phosphoinositide-3-kinase, regulatory subunit 2 (beta)	19q13.2-q13.4	5296	BC033311
207081_s_at	PI4KA	phosphatidylinositol 4-kinase, catalytic, alpha	22q11.21	5297	NM_002650
206139_at	PI4KB	phosphatidylinositol 4-kinase, catalytic, beta	1q21	5298	NM_002651
212829_at	PIP4K2A	phosphatidylinositol-5-phosphate 4-kinase, type II, alpha	10p12.2	5305	BE878277

201251_at	PKM2	pyruvate kinase, muscle	15q22	5315	NM_002654
205406_s_at	SPA17	sperm autoantigenic protein 17	11q24.2	53340	NM_017425
226649_at	PANK1	pantothenate kinase 1	10q23.31	53354	AI373299
202240_at	PLK1	polo-like kinase 1 (Drosophila)	16p12.1	5347	NM_005030
223904_at	PRKAG3	protein kinase, AMP-activated, gamma 3 non-catalytic subur	2q35	53632	AF214519
207541_s_at	EXOSC10	exosome component 10	1p36.22	5394	NM_002685
231920_s_at	CSNK1G1	casein kinase 1, gamma 1	5q22.1-q22.3	53944	AK025179
221215_s_at	RIPK4	receptor-interacting serine-threonine kinase 4	21q22.3	54101	NM_020639
209902_at	ATR	ataxia telangiectasia and Rad3 related	3q22-q24	545	U49844
223324_s_at	TRPM7	transient receptor potential cation channel, subfamily M, me	15q21	54822	AF346629
207474_at	SNRK	SNF related kinase	3p22.1	54861	NM_017719
1552275_s_at	PXK	PX domain containing serine/threonine kinase	3p14.3	54899	BG573647
218533_s_at	UCKL1	uridine-cytidine kinase 1-like 1	20q13.33	54963	NM_017859
208652_at	PPP2CA	protein phosphatase 2 (formerly 2A), catalytic subunit, alpha	5q31.1	5515	BC000400
201375_s_at	PPP2CB	protein phosphatase 2 (formerly 2A), catalytic subunit, beta	8p12	5516	NM_004156
218209_s_at	RPRD1A	regulation of nuclear pre-mRNA domain containing 1A	18q12.2	55197	NM_018170
218771_at	PANK4	pantothenate kinase 4	1p36.32	55229	NM_018216
208260_at	AVPR1B	arginine vasopressin receptor 1B	1q32	553	NM_000707
222631_at	PI4K2B	phosphatidylinositol 4-kinase type 2 beta	4p15.2	55300	AI862887
208932_at	PPP4C	protein phosphatase 4 (formerly X), catalytic subunit	16p12-p11	5531	BC001416
219686_at	STK32B	serine/threonine kinase 32B	4p16.2-p16.1	55351	NM_018401
220030_at	STYK1	serine/threonine/tyrosine kinase 1	12p13.2	55359	NM_018423
209345_s_at	PI4K2A	phosphatidylinositol 4-kinase type 2 alpha	10q24	55361	AL561930
223266_at	STRADB	STE20-related kinase adaptor beta	2q33.1	55437	AB038950
218231_at	NAGK	N-acetylglucosamine kinase	2p13.3	55577	NM_017567
59644_at	BMP2K	BMP2 inducible kinase	4q21.21	55589	AI735391
214917_at	PRKAA1	protein kinase, AMP-activated, alpha 1 catalytic subunit	5p12	5562	AK024252
227892_at	PRKAA2	protein kinase, AMP-activated, alpha 2 catalytic subunit	1p31	5563	AA855042
202801_at	PRKACA	protein kinase, cAMP-dependent, catalytic, alpha	19p13.1	5566	NM_002730
202742_s_at	PRKACB	protein kinase, cAMP-dependent, catalytic, beta	1p36.1	5567	NM_002731
204612_at	PKIA	protein kinase (cAMP-dependent, catalytic) inhibitor alpha	8q21.12	5569	NM_006823
223551_at	PKIB	protein kinase (cAMP-dependent, catalytic) inhibitor beta	6q22.31	5570	AF225513
201805_at	PRKAG1	protein kinase, AMP-activated, gamma 1 non-catalytic subur	12q12-q14	5571	NM_002733
200604_s_at	PRKAR1A	protein kinase, cAMP-dependent, regulatory, type I, alpha (ti	17q23-q24	5573	M18468
225011_at	PRKAR2A	protein kinase, cAMP-dependent, regulatory, type II, alpha	3p21.3-p21.2	5576	AK026351
203680_at	PRKAR2B	protein kinase, cAMP-dependent, regulatory, type II, beta	7q22	5577	NM_002736
213093_at	PRKCA	protein kinase C, alpha	17q22-q23.2	5578	AI471375
209685_s_at	PRKCB	protein kinase C, beta	16p11.2	5579	M13975
202686_s_at	AXL	AXL receptor tyrosine kinase	19q13.1	558	NM_021913
202545_at	PRKCD	protein kinase C, delta	3p21.31	5580	NM_006254

226101_at	PRKCE	protein kinase C, epsilon	2p21	5581	AI093546
218764_at	PRKCH	protein kinase C, eta	14q22-q23	5583	NM_024064
213518_at	PRKCI	protein kinase C, iota	3q26.3	5584	AI689429
202161_at	PKN1	protein kinase N1	19p13.1-p12	5585	NM_002741
212629_s_at	PKN2	protein kinase N2	1p22.2	5586	AI633689
205880_at	PRKD1	protein kinase D1	14q11	5587	NM_002742
219148_at	PBK	PDZ binding kinase	8p21.2	55872	NM_018492
210038_at	PRKCQ	protein kinase C, theta	10p15	5588	AL137145
200707_at	PRKCSH	protein kinase C substrate 80K-H	19p13.2	5589	NM_002743
202178_at	PRKCZ	protein kinase C, zeta	1p36.33-p36.2	5590	NM_002744
210543_s_at	PRKDC	protein kinase, DNA-activated, catalytic polypeptide	8q11	5591	U34994
228396_at	PRKG1	protein kinase, cGMP-dependent, type I	10q11.2	5592	AW274503
212271_at	MAPK1	mitogen-activated protein kinase 1	q11.2|22q11.	5594	AA195999
212046_x_at	MAPK3	mitogen-activated protein kinase 3	16p11.2	5595	X60188
207121_s_at	MAPK6	mitogen-activated protein kinase 6	15q21	5597	NM_002748
35617_at	MAPK7	mitogen-activated protein kinase 7	17p11.2	5598	U29725
226048_at	MAPK8	mitogen-activated protein kinase 8	10q11.22	5599	N92719
211499_s_at	MAPK11	mitogen-activated protein kinase 11	22q13.33	5600	U92268
203218_at	MAPK9	mitogen-activated protein kinase 9	5q35	5601	W37431
204813_at	MAPK10	mitogen-activated protein kinase 10	4q22.1-q23	5602	NM_002753
210058_at	MAPK13	mitogen-activated protein kinase 13	6p21.31	5603	BC000433
202670_at	MAP2K1	mitogen-activated protein kinase kinase 1	5q22.1-q22.3	5604	AI571419
202424_at	MAP2K2	mitogen-activated protein kinase kinase 2	19p13.3	5605	NM_030662
215498_s_at	MAP2K3	mitogen-activated protein kinase kinase 3	17q11.2	5606	AA780381
216765_at	MAP2K5	mitogen-activated protein kinase kinase 5	15q23	5607	AK025177
205698_s_at	MAP2K6	mitogen-activated protein kinase kinase 6	17q24.3	5608	NM_002758
226053_at	MAP2K7	mitogen-activated protein kinase kinase 7	19p13.3-p13.2	5609	AI090153
204211_x_at	EIF2AK2	eukaryotic translation initiation factor 2-alpha kinase 2	2p22-p21	5610	NM_002759
235341_at	DNAJC3	DnaJ (Hsp40) homolog, subfamily C, member 3	13q32	5611	AL119957
204061_at	PRKX	protein kinase, X-linked	Xp22.3	5613	NM_005044
221035_s_at	TEX14	testis expressed 14	17q22	56155	NM_031272
208447_s_at	PRPS1	phosphoribosyl pyrophosphate synthetase 1	Xq21.32-q24	5631	NM_002764
230352_at	PRPS2	phosphoribosyl pyrophosphate synthetase 2	Xp22.3-p22.2	5634	AI392908
1556715_at	PRPSAP1	phosphoribosyl pyrophosphate synthetase-associated proteir	17q24-q25	5635	N40988
203537_at	PRPSAP2	phosphoribosyl pyrophosphate synthetase-associated proteir	17p11.2-p12	5636	NM_002767
214575_s_at	AZU1	azurocidin 1	19p13.3	566	NM_001700
213141_at	PSKH1	protein serine kinase H1	16q22.1	5681	AJ272212
40273_at	SPHK2	sphingosine kinase 2	19q13.2	56848	AA485440
1555310_a_at	PAK6	p21 protein (Cdc42/Rac)-activated kinase 6	15q14	56924	BC035596
218845_at	DUSP22	dual specificity phosphatase 22	6p25.3	56940	NM_020185

229026_at	CDC42SE2	CDC42 small effector 2	5q31.1	56990	BE675995
220246_at	CAMK1D	calcium/calmodulin-dependent protein kinase ID	10p13	57118	NM_020397
227482_at	ADCK1	aarF domain containing kinase 1	14q24.3	57143	AI097656
213990_s_at	PAK7	p21 protein (Cdc42/Rac)-activated kinase 7	20p12	57144	BF056517
41329_at	SCYL3	SCY1-like 3 (S. cerevisiae)	1q24.2	57147	AI458463
241403_at	CLK4	CDC-like kinase 4	5q35	57396	AA468591
223033_s_at	SCYL1	SCY1-like 1 (S. cerevisiae)	11q13	57410	AF297709
1559529_at	PTK2	PTK2 protein tyrosine kinase 2	8q24-qter	5747	BC043202
206482_at	PTK6	PTK6 protein tyrosine kinase 6	20q13.3	5753	NM_005975
228342_s_at	ALPK3	alpha-kinase 3	15q25.2	57538	AA843297
207011_s_at	PTK7	PTK7 protein tyrosine kinase 7	6p21.1-p12.2	5754	NM_002821
227454_at	TAOK1	TAO kinase 1	17q11.2	57551	AB037782
214007_s_at	TWF1	twinfilin, actin-binding protein, homolog 1 (Drosophila)	12q12	5756	AW665024
230112_at	MARCH4	membrane-associated ring finger (C3HC4) 4	2q35	57574	AB037820
218145_at	TRIB3	tribbles homolog 3 (Drosophila)	20p13-p12.2	57761	NM_021158
55065_at	MARK4	MAP/microtubule affinity-regulating kinase 4	19q13.3	57787	AL120554
1569323_at	PTPRG	protein tyrosine phosphatase, receptor type, G	3p21-p14	5793	BU853579
227396_at	PTPRJ	protein tyrosine phosphatase, receptor type, J	11p11.2	5795	AI631833
217791_s_at	ALDH18A1	aldehyde dehydrogenase 18 family, member A1	10q24.3	5832	NM_002860
204936_at	MAP4K2	mitogen-activated protein kinase kinase kinase kinase 2	11q13	5871	NM_004579
1567458_s_at	RAC1	ras-related C3 botulinum toxin substrate 1 (rho family, small	7p22	5879	AJ012502
205130_at	RAGE	renal tumor antigen	14q32	5891	NM_014226
1557675_at	RAF1	v-raf-1 murine leukemia viral oncogene homolog 1	3p25	5894	BI496583
228109_at	RASGRF2	Ras protein-specific guanine nucleotide-releasing factor 2	5q13	5924	AI912976
211421_s_at	RET	ret proto-oncogene	10q11.2	5979	M31213
210541_s_at	TRIM27	tripartite motif-containing 27	6p22	5987	AF230394
229285_at	RNASEL	ribonuclease L (2',5'-oligoisoadenylate synthetase-dependen	1q25	6041	AI669749
214911_s_at	BRD2	bromodomain containing 2	6p21.3	6046	S78771
214578_s_at	ROCK1	Rho-associated, coiled-coil containing protein kinase 1	18q11.1	6093	AV683882
205191_at	RP2	retinitis pigmentosa 2 (X-linked recessive)	(p11.4-p11.21	6102	NM_006915
202315_s_at	BCR	breakpoint cluster region	2q11|22q11.2	613	NM_004327
203379_at	RPS6KA1	ribosomal protein S6 kinase, 90kDa, polypeptide 1	1p	6195	NM_002953
212912_at	RPS6KA2	ribosomal protein S6 kinase, 90kDa, polypeptide 2	6q27	6196	AI992251
203843_at	RPS6KA3	ribosomal protein S6 kinase, 90kDa, polypeptide 3	Xp22.2-p22.1	6197	AA906056
226660_at	RPS6KB1	ribosomal protein S6 kinase, 70kDa, polypeptide 1	17q23.1	6198	AI142096
203777_s_at	RPS6KB2	ribosomal protein S6 kinase, 70kDa, polypeptide 2	11q13.1	6199	NM_003952
205870_at	BDKRB2	bradykinin receptor B2	14q32.1-q32.2	624	NM_000623
216976_s_at	RYK	RYK receptor-like tyrosine kinase	3q22	6259	X96588
206106_at	MAPK12	mitogen-activated protein kinase 12	22q13.33	6300	AL022328
216598_s_at	CCL2	chemokine (C-C motif) ligand 2	17q11.2-q12	6347	S69738

204103_at	CCL4	chemokine (C-C motif) ligand 4	17q12	6351	NM_002984
206255_at	BLK	B lymphoid tyrosine kinase	8p23-p22	640	NM_001715
57540_at	RBKS	ribokinase	2p23.3	64080	AI823980
203265_s_at	MAP2K4	mitogen-activated protein kinase kinase 4	17p11.2	6416	AA810268
201739_at	SGK1	serum/glucocorticoid regulated kinase 1	6q23	6446	NM_005627
201469_s_at	SHC1	SHC (Src homology 2 domain containing) transforming prote	1q21	6464	AI809967
219092_s_at	IPPK	inositol 1,3,4,5,6-pentakisphosphate 2-kinase	q21.33-q22.3	64768	NM_022755
218421_at	CERK	ceramide kinase	22q13.31	64781	NM_022766
209018_s_at	PINK1	PTEN induced putative kinase 1	1p36	65018	BF432478
39313_at	WNK1	WNK lysine deficient protein kinase 1	12p13.3	65125	AB002342
229158_at	WNK4	WNK lysine deficient protein kinase 4	17q21-q22	65266	AW082836
232282_at	WNK3	WNK lysine deficient protein kinase 3	p11.23-p11.2	65267	H06509
227217_at	WNK2	WNK lysine deficient protein kinase 2	9q22.3	65268	AI637586
213578_at	BMPR1A	bone morphogenetic protein receptor, type IA	10q22.3	657	AI678679
210523_at	BMPR1B	bone morphogenetic protein receptor, type IB	4q22-q24	658	D89675
231873_at	BMPR2	bone morphogenetic protein receptor, type II (serine/threoni	2q33-q34	659	AL046696
206464_at	BMX	BMX non-receptor tyrosine kinase	Xp22.2	660	NM_001721
213324_at	SRC	v-src sarcoma (Schmidt-Ruppin A-2) viral oncogene homolog	20q12-q13	6714	AK024281
243829_at	BRAF	v-raf murine sarcoma viral oncogene homolog B1	7q34	673	AW613053
202200_s_at	SRPK1	SFRS protein kinase 1	6p21.3-p21.2	6732	NM_003137
1558254_s_at	SRPK2	SFRS protein kinase 2	7q22-q31.1	6733	BU155802
204634_at	NEK4	NIMA (never in mitosis gene a)-related kinase 4	3p21.1	6787	NM_003157
204068_at	STK3	serine/threonine kinase 3 (STE20 homolog, yeast)	8q22.2	6788	NM_006281
243981_at	STK4	serine/threonine kinase 4	20q11.2-q13.2	6789	AI763206
208079_s_at	AURKA	aurora kinase A	20q13.2-q13.3	6790	NM_003158
40420_at	STK10	serine/threonine kinase 10	5q35.1	6793	AB015718
231017_at	STK11	serine/threonine kinase 11	19p13.3	6794	AI914604
211107_s_at	AURKC	aurora kinase C	19q13.43	6795	AB017332
244023_at	SYK	spleen tyrosine kinase	9q22	6850	AW467357
216711_s_at	TAF1	TAF1 RNA polymerase II, TATA box binding protein (TBP)-ass	Xq13.1	6872	M73444
206853_s_at	MAP3K7	mitogen-activated protein kinase kinase kinase 7	6q16.1-q16.3	6885	AL121964
205504_at	BTK	Bruton agammaglobulinemia tyrosine kinase	Xq21.33-q22	695	NM_000061
209642_at	BUB1	budding uninhibited by benzimidazoles 1 homolog (yeast)	2q14	699	AF043294
203755_at	BUB1B	budding uninhibited by benzimidazoles 1 homolog beta (yea	15q15	701	NM_001211
206702_at	TEK	TEK tyrosine kinase, endothelial	9p21	7010	NM_000459
204106_at	TESK1	testis-specific kinase 1	9p13	7016	NM_006285
224793_s_at	TGFBR1	transforming growth factor, beta receptor 1	9q22	7046	AA604375
208944_at	TGFBR2	transforming growth factor, beta receptor II (70/80kDa)	3p22	7048	D50683
204468_s_at	TIE1	tyrosine kinase with immunoglobulin-like and EGF-like doma	1p34-p33	7075	NM_005424
1554408_a_at	TK1	thymidine kinase 1, soluble	17q23.2-q25.3	7083	BC007986

204276_at	TK2	thymidine kinase 2, mitochondrial	16q22-q23.1	7084	BE895437
210176_at	TLR1	toll-like receptor 1	4p14	7096	AL050262
206271_at	TLR3	toll-like receptor 3	4q35	7098	NM_003265
221060_s_at	TLR4	toll-like receptor 4	9q32-q33	7099	NM_003266
231403_at	TRIO	triple functional domain (PTPRF interacting)	5p15.2	7204	N21108
204822_at	TTK	TTK protein kinase	6q13-q21	7272	NM_003318
208195_at	TTN	titin	2q31	7273	NM_003319
212401_s_at	CDC2L2	cell division cycle 2-like 2 (PITSLRE proteins)	1p36.33	728642	AI767436
205546_s_at	TYK2	tyrosine kinase 2	19p13.2	7297	NM_003331
211432_s_at	TYRO3	TYRO3 protein tyrosine kinase	15q15.1-q21.1	7301	U05682
232180_at	UGP2	UDP-glucose pyrophosphorylase 2	2p14-p13	7360	U00954
209825_s_at	UCK2	uridine-cytidine kinase 2	1q23	7371	BC002906
203856_at	VRK1	vaccinia related kinase 1	14q32	7443	NM_003384
205126_at	VRK2	vaccinia related kinase 2	2p16-p15	7444	NM_006296
215711_s_at	WEE1	WEE1 homolog (S. pombe)	11p15.3-p15.1	7465	AJ277546
202932_at	YES1	v-yes-1 Yamaguchi sarcoma viral oncogene homolog 1	3p11.31-p11.2	7525	NM_005433
242325_at	YWHAH	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase ac	22q12.3	7533	AA909983
1555613_a_at	ZAP70	zeta-chain (TCR) associated protein kinase 70kDa	2q12	7535	AB083211
205447_s_at	MAP3K12	mitogen-activated protein kinase kinase kinase 12	12q13	7786	BE222201
1007_s_at	DDR1	discoidin domain receptor tyrosine kinase 1	6p21.3	780	U48705
202788_at	MAPKAPK3	mitogen-activated protein kinase-activated protein kinase 3	3p21.3	7867	NM_004635
219365_s_at	CAMKV	CaM kinase-like vesicle-associated	3p21.31	79012	NM_024046
220599_s_at	CARD14	caspase recruitment domain family, member 14	17q25	79092	NM_024110
218433_at	PANK3	pantothenate kinase 3	5q34	79646	NM_024594
218210_at	FN3KRP	fructosamine-3-kinase-related protein	17q25.3	79672	NM_024619
218942_at	PIP4K2C	phosphatidylinositol-5-phosphate 4-kinase, type II, gamma	12q13.3	79837	NM_024779
219542_at	NEK11	NIMA (never in mitosis gene a)- related kinase 11	3q22.1	79858	NM_024800
220434_at	ADCK4	aarF domain containing kinase 4	19q13.2	79934	NM_024876
213076_at	ITPKC	inositol 1,4,5-trisphosphate 3-kinase C	19q13.1	80271	D38169
218740_s_at	CDK5RAP3	CDK5 regulatory subunit associated protein 3	17q21.32	80279	NM_025197
219986_s_at	ACAD10	acyl-Coenzyme A dehydrogenase family, member 10	12q24.12	80724	NM_025247
200623_s_at	CALM3	calmodulin 3 (phosphorylase kinase, delta)	19q13.2-q13.3	808	NM_005184
221548_s_at	ILKAP	integrin-linked kinase-associated serine/threonine phosphat	2q37.3	80895	AY024365
209956_s_at	CAMK2B	calcium/calmodulin-dependent protein kinase II beta	12|7p14.3-p1	816	U23460
233647_s_at	CDADC1	cytidine and dCMP deaminase domain containing 1	13q14.2	81602	AL138875
1556560_a_at	TSSK3	testis-specific serine kinase 3	1p35-p34	81629	BI825578
210625_s_at	AKAP1	A kinase (PRKA) anchor protein 1	17q21-q23	8165	U34074
231793_s_at	CAMK2D	calcium/calmodulin-dependent protein kinase II delta	4q26	817	AA448956
214322_at	CAMK2G	calcium/calmodulin-dependent protein kinase II gamma	10q22	818	AA284757
204510_at	CDC7	cell division cycle 7 homolog (S. cerevisiae)	1p22	8317	NM_003503

223142_s_at	UCK1	uridine-cytidine kinase 1	9q34.13	83549	AF237290
223534_s_at	RPS6KL1	ribosomal protein S6 kinase-like 1	14q24.3	83694	BC004540
224450_s_at	RIOK1	RIO kinase 1 (yeast)	6p24.3	83732	BC006104
206197_at	NME5	non-metastatic cells 5, protein expressed in (nucleoside-diph	5q31	8382	NM_003551
223759_s_at	GSG2	germ cell associated 2 (haspin)	17p13	83903	AB039834
223852_s_at	STK40	serine/threonine kinase 40	1p34.3	83931	BC005169
207391_s_at	PIP5K1A	phosphatidylinositol-4-phosphate 5-kinase, type I, alpha	1q22-q24	8394	NM_003557
201080_at	PIP4K2B	phosphatidylinositol-5-phosphate 4-kinase, type II, beta	17q12	8396	BF338509
229854_at	OBSCN	obscurin, cytoskeletal calmodulin and titin-interacting RhoGE	1q42.13	84033	AW614056
209333_at	ULK1	unc-51-like kinase 1 (C. elegans)	12q24.3	8408	AB018265
225165_at	PPP1R1B	protein phosphatase 1, regulatory (inhibitor) subunit 1B	17q12	84152	AK024593
223460_at	CAMKK1	calcium/calmodulin-dependent protein kinase kinase 1, alph	17p13.2	84254	AL136576
215188_at	STK24	serine/threonine kinase 24 (STE20 homolog, yeast)	13q31.2-q32.3	8428	AF339785
210151_s_at	DYRK3	dual-specificity tyrosine-(Y)-phosphorylation regulated kinase	1q32.1	8444	AF186773
1552504_a_at	BRSK1	BR serine/threonine kinase 1	19q13.4	84446	NM_032430
202971_s_at	DYRK2	dual-specificity tyrosine-(Y)-phosphorylation regulated kinase	12q15	8445	NM_006482
228565_at	KIAA1804	mixed lineage kinase 4	1q42	84451	AI809005
230191_at	TTBK1	tau tubulin kinase 1	6p21.1	84630	H04790
214464_at	CDC42BPA	CDC42 binding protein kinase alpha (DMPK-like)	1q42.11	8476	NM_003607
218311_at	MAP4K3	mitogen-activated protein kinase kinase kinase kinase 3	2p22.1	8491	NM_003618
202743_at	PIK3R3	phosphoinositide-3-kinase, regulatory subunit 3 (gamma)	1p34.1	8503	BE622627
202491_s_at	IKBKAP	inhibitor of kappa light polypeptide gene enhancer in B-cells,	9q31	8518	NM_003640
207556_s_at	DGKZ	diacylglycerol kinase, zeta 104kDa	11p11.2	8525	NM_003646
208072_s_at	DGKD	diacylglycerol kinase, delta 130kDa	2q37.1	8527	NM_003648
1558556_at	CAMK1	calcium/calmodulin-dependent protein kinase I	3p25.3	8536	AL041824
231792_at	MYLK2	myosin light chain kinase 2	20q13.31	85366	AF325549
212871_at	MAPKAPK5	mitogen-activated protein kinase-activated protein kinase 5	12q24.12-q24.1	8550	NM_003668
203468_at	CDK10	cyclin-dependent kinase 10	16q24	8558	NM_003674
218019_s_at	PDXK	pyridoxal (pyridoxine, vitamin B6) kinase	21q22.3	8566	NM_021941
1560720_at	MKNK1	MAP kinase interacting serine/threonine kinase 1	1p33	8569	AI023699
207620_s_at	CASK	calcium/calmodulin-dependent serine protein kinase (MAGU	Xp11.4	8573	NM_003688
237107_at	PRKRA	protein kinase, interferon-inducible double stranded RNA de	2q31.2	8575	AA279462
209622_at	STK16	serine/threonine kinase 16	2q34-q37	8576	AB020739
207319_s_at	CDC2L5	cell division cycle 2-like 5 (cholinesterase-related cell divisio	7p13	8621	NM_003718
205790_at	SKAP1	src kinase associated phosphoprotein 1	17q21.32	8631	NM_003726
217971_at	MAPKSP1	MAPK scaffold protein 1	4q23	8649	NM_021970
210001_s_at	SOCS1	suppressor of cytokine signaling 1	16p13.13	8651	AB005043
217149_x_at	TNK1	tyrosine kinase, non-receptor, 1	17p13.1	8711	AF097738
209941_at	RIPK1	receptor (TNFRSF)-interacting serine-threonine kinase 1	6p25.2	8737	U50062
1555326_a_at	ADAM9	ADAM metallopeptidase domain 9 (meltrin gamma)	8p11.23	8754	AF495383

209545_s_at	RIPK2	receptor-interacting serine-threonine kinase 2	8q21	8767	AF064824
202129_s_at	RIOK3	RIO kinase 3 (yeast)	18q11.2	8780	AW006290
231775_at	TNFRSF10A	tumor necrosis factor receptor superfamily, member 10a	8p21	8797	W65310
212954_at	DYRK4	dual-specificity tyrosine-(Y)-phosphorylation regulated kinas	12p13.32	8798	AF263541
204995_at	CDK5R1	cyclin-dependent kinase 5, regulatory subunit 1 (p35)	17q11.2	8851	AL567411
204090_at	STK19	serine/threonine kinase 19	6p21.3	8859	NM_004197
219257_s_at	SPHK1	sphingosine kinase 1	17q25.2	8877	NM_021972
244804_at	SQSTM1	sequestosome 1	5q35	8878	AW293441
211090_s_at	PRPF4B	PRP4 pre-mRNA processing factor 4 homolog B (yeast)	6p25.2	8899	Z25435
205852_at	CDK5R2	cyclin-dependent kinase 5, regulatory subunit 2 (p39)	2q35	8941	R51311
204632_at	RPS6KA4	ribosomal protein S6 kinase, 90kDa, polypeptide 4	11q11-q13	8986	NM_003942
227750_at	KALRN	kalirin, RhoGEF kinase	3q21.1-q21.2	8997	AL137629
203935_at	ACVR1	activin A receptor, type I	2q23-q24	90	NM_001105
210087_s_at	MPZL1	myelin protein zero-like 1	1q24.2	9019	AF095727
205192_at	MAP3K14	mitogen-activated protein kinase kinase kinase 14	17q21	9020	NM_003954
223715_at	BRSK2	BR serine/threonine kinase 2	11p15.5	9024	AF020089
203060_s_at	PAPSS2	3'-phosphoadenosine 5'-phosphosulfate synthase 2	10q23-q24	9060	AF074331
209043_at	PAPSS1	3'-phosphoadenosine 5'-phosphosulfate synthase 1	4q24	9061	AF033026
219278_at	MAP3K6	mitogen-activated protein kinase kinase kinase 6	1p36.11	9064	NM_004672
204267_x_at	PKMYT1	protein kinase, membrane associated tyrosine/threonine 1	16p13.3	9088	NM_004203
221893_s_at	ADCK2	aarF domain containing kinase 2	7q32-q34	90956	N32831
205209_at	ACVR1B	activin A receptor, type IB	12q13	91	BC000254
217270_s_at	DYRK1B	dual-specificity tyrosine-(Y)-phosphorylation regulated kinas	19q12-q13.1	9149	AC005393
205456_at	CD3E	CD3e molecule, epsilon (CD3-TCR complex)	11q23	916	NM_000733
1562440_at	MAP3K13	mitogen-activated protein kinase kinase kinase 13	3q27	9175	BC026249
212299_at	NEK9	NIMA (never in mitosis gene a)- related kinase 9	14q24.3	91754	AL117502
228416_at	ACVR2A	activin A receptor, type IIA	2q22.3	92	AI149508
203547_at	CD4	CD4 molecule	12pter-p12	920	U47924
205399_at	DCLK1	doublecortin-like kinase 1	13q13	9201	NM_004734
209464_at	AURKB	aurora kinase B	17p13.1	9212	AB011446
221554_at	STRADA	STE20-related kinase adaptor alpha	17q23.3	92335	AF308302
214551_s_at	CD7	CD7 molecule	17q25.2-q25.3	924	NM_006137
204635_at	RPS6KA5	ribosomal protein S6 kinase, 90kDa, polypeptide 5	14q31-q32.1	9252	NM_004755
201461_s_at	MAPKAPK2	mitogen-activated protein kinase-activated protein kinase 2	1q32	9261	NM_004759
205214_at	STK17B	serine/threonine kinase 17b	2q32.3	9262	NM_004226
202693_s_at	STK17A	serine/threonine kinase 17a	7p12-p14	9263	AW194730
203336_s_at	ITGB1BP1	integrin beta 1 binding protein 1	2p25.2	9270	AL548363
201098_at	COPB2	coatomer protein complex, subunit beta 2 (beta prime)	3q23	9276	NM_004766
220028_at	ACVR2B	activin A receptor, type IIB	3p22	93	NM_001106
204986_s_at	TAOK2	TAO kinase 2	16p11.2	9344	NM_016151

226126_at	MGC16169	hypothetical protein MGC16169	4q24	93627	AA702160
226950_at	ACVRL1	activin A receptor type II-like 1	12q11-q14	94	T63524
232017_at	TJP2	tight junction protein 2 (zona occludens 2)	9q13-q21	9414	AK025185
1558732_at	MAP4K4	mitogen-activated protein kinase kinase kinase kinase 4	2q11.2-q12	9448	AK074900
218696_at	EIF2AK3	eukaryotic translation initiation factor 2-alpha kinase 3	2p12	9451	NM_004836
204746_s_at	PICK1	protein interacting with PRKCA 1	22q13.1	9463	NM_012407
205771_s_at	AKAP7	A kinase (PRKA) anchor protein 7	6q23	9465	AL137063
202762_at	ROCK2	Rho-associated, coiled-coil containing protein kinase 2	2p24	9475	AL049383
213013_at	MAPK8IP1	mitogen-activated protein kinase 8 interacting protein 1	11p12-p11.2	9479	BG164295
230846_at	AKAP5	A kinase (PRKA) anchor protein 5	14q21-q24	9495	R43202
204220_at	GMFG	glia maturation factor, gamma	19q13.2	9535	NM_004877
217849_s_at	CDC42BPB	CDC42 binding protein kinase beta (DMPK-like)	14q32.3	9578	NM_006035
205986_at	AATK	apoptosis-associated tyrosine kinase	17q25.3	9625	NM_004920
214398_s_at	IKBKE	inhibitor of kappa light polypeptide gene enhancer in B-cells,	1q32.1	9641	AW340333
208127_s_at	SOCS5	suppressor of cytokine signaling 5	2p21	9655	NM_014011
204062_s_at	ULK2	unc-51-like kinase 2 (C. elegans)	17p11.2	9706	BG526973
206875_s_at	SLK	STE20-like kinase (yeast)	10q25.1	9748	NM_014720
212439_at	IHPK1	inositol hexaphosphate kinase 1	3p21.31	9807	BE614199
210559_s_at	CDC2	cell division cycle 2, G1 to S and G2 to M	10q21.1	983	D88357
204825_at	MELK	maternal embryonic leucine zipper kinase	9p13.2	9833	NM_014791
210474_s_at	CDC2L1	cell division cycle 2-like 1 (PITSLRE proteins)	1p36.33	984	U04819
210379_s_at	TLK1	tousled-like kinase 1	2q31.1	9874	AF162666
204589_at	NUAK1	NUAK family, SNF1-like kinase, 1	12q23.3	9891	NM_014840
37408_at	MRC2	mannose receptor, C type 2	17q23.2	9902	AB014609

Supplementary Table S2: list of the 36 selected probesets and their prognostic values in HM UAMS-TT2 and UAMS-TT3 cohorts.

			HM					UAMS-TT2				UAMS-TT3			
PROBESET-AFFYM	Name	Prognostic	Maxstat_Cut	Chisq	pvalue	multiple corr	Hazard_Ratio	Maxstat_Cut	Chisq	pvalue	Hazard_Ratio	Maxstat_Cut	Chisq	pvalue	Hazard_Ratio
1007_s_at	DDR1	Good	232	21	5.10E-06	1.69E-03	0.23	264	13	3.20E-04	0.42	334.2	6.2	1.30E-02	0.23
1554408_a_at	TK1	Bad	162	10	1.30E-03	1.72E-02	3.2	826	16	7.30E-05	2.5	492.5	7.1	7.70E-03	5.2
1555758_a_at	CDKN3	Bad	313	9.9	1.70E-03	2.04E-02	2.8	772	16	7.70E-05	2.2	1129.8	10	1.50E-03	6.1
1558254_s_at	SRPK2	Bad	356	7.9	5.00E-03	3.80E-02	2.8	666	6.3	1.20E-02	1.6	963.1	11	1.10E-03	6.3
1559052_s_at	PAK2	Bad	345	17	3.80E-05	2.28E-03	4.1	858	12	5.40E-04	2.1	872.1	7	8.10E-03	4.7
1569323_at	PTPRG	Bad	17	7.4	6.50E-03	4.48E-02	5.7	135	4	4.50E-02	1.5	207.1	12	4.30E-04	7
200707_at	PRKCSH	Good	386	7.1	7.70E-03	4.89E-02	0.42	4078	5.1	2.40E-02	0.47	1978.3	5.9	1.60E-02	0.24
201037_at	PFKP	Bad	415	7.9	4.90E-03	3.77E-02	2.9	244	6.3	1.20E-02	1.9	151	5.2	2.20E-02	3.9
201897_s_at	CKS1B	Bad	3589	14	1.80E-04	4.76E-03	3.8	2447	20	6.40E-06	2.8	2334	6.3	1.20E-02	4.4
202200_s_at	SRPK1	Bad	2670	10	1.40E-03	1.78E-02	3	2773	4.7	2.90E-02	1.7	2333	9.2	2.50E-03	5.7
202284_s_at	CDKN1A	Good	2647	14	2.10E-04	5.14E-03	0.32	1579	9.7	1.90E-03	0.46	1481	20	8.70E-06	0.1
202786_at	STK39	Bad	1176	9.7	1.90E-03	2.17E-02	2.9	429	7	8.40E-03	1.6	1041.5	7.8	5.20E-03	5.1
202934_at	HK2	Bad	1887	7.3	7.10E-03	4.79E-02	2.3	1079	11	8.40E-04	1.9	1607.6	7.4	6.40E-03	4.9
203755_at	BUB1B	Bad	1386	18	2.20E-05	2.08E-03	4	1328	14	1.90E-04	2.3	1173.1	17	3.80E-05	10
204159_at	CDKN2C	Bad	1936	9.4	2.20E-03	2.42E-02	3	1184	6.5	1.10E-02	1.7	1602.3	12	5.60E-04	6.6
204170_s_at	CKS2	Bad	3540	10	1.30E-03	1.75E-02	2.7	3334	5.7	1.70E-02	1.6	2952.1	14	1.90E-04	720
204244_s_at	DBF4	Bad	3149	18	2.30E-05	1.69E-03	3.5	1338	8.8	2.90E-03	1.8	1442.1	5.3	2.10E-02	4
204510_at	CDC7	Bad	283	7.1	7.60E-03	4.93E-02	2.4	585	11	7.30E-04	2.2	457.2	11	1.10E-03	6.3
204641_at	NEK2	Bad	371	22	2.50E-06	1.65E-03	3.9	889	31	2.10E-08	3.4	752.3	14	1.60E-04	7.6
204822_at	TTK	Bad	322	20	8.60E-06	1.89E-03	4	569	17	4.50E-05	2.4	608.2	12	6.40E-04	6.5
204825_at	MELK	Bad	2350	12	6.80E-04	1.15E-02	3.2	859	5.9	1.50E-02	1.6	1538.9	7.9	4.90E-03	5.1
204887_s_at	PLK4	Bad	318	16	6.50E-05	3.58E-03	3.4	495	13	2.70E-04	2.3	414.4	16	7.10E-05	8.6
204936_at	MAP4K2	Good	16	7.9	4.90E-03	3.81E-02	0.36	25	6.6	1.00E-02	0.61	35.1	5.4	2.10E-02	0.25
205394_at	CHEK1	Bad	617	17	3.00E-05	1.98E-03	3.7	553	17	4.10E-05	2.6	573.7	15	1.00E-04	8.2
205486_at	TESK2	Good	604	7.6	5.90E-03	4.15E-02	0.39	826	17	2.90E-05	0.46	528.4	10	1.30E-03	0.16
205698_s_at	MAP2K6	Bad	440	7.1	7.60E-03	4.88E-02	4.3	412	6.7	9.40E-03	2.5	581.4	7	8.10E-03	9.7
205936_s_at	HK3	Good	29	7.5	6.20E-03	4.31E-02	0.41	34	9.7	1.90E-03	0.51	19	11	1.10E-03	0.16
208079_s_at	AURKA	Bad	324	16	6.80E-05	3.21E-03	3.3	71	8.5	3.50E-03	3	456.6	9.7	1.80E-03	5.7
209642_at	BUB1	Bad	359	16	6.60E-05	3.36E-03	3.3	843	14	2.00E-04	2.2	1060.1	10	1.20E-03	6.2
211913_s_at	MERTK	Good	370	10	1.40E-03	1.81E-02	0.34	588	8.2	4.30E-03	0.59	347.4	12	6.40E-04	0.13
214575_s_at	AZU1	Good	72	8.6	3.30E-03	2.99E-02	0.36	97	4.6	3.10E-02	0.52	24.8	8.6	3.40E-03	0.18
215025_at	NTRK3	Bad	123	16	7.40E-05	3.26E-03	3.3	98	7	8.10E-03	1.6	229.7	5.1	2.40E-02	4.2
218209_s_at	RPRD1A	Bad	1912	20	9.20E-06	1.52E-03	4.8	1837	6.3	1.20E-02	1.8	1576.9	6.7	9.80E-03	4.6
219148_at	PBK	Bad	441	14	2.30E-04	5.43E-03	3.1	762	13	2.70E-04	2.4	748.7	11	7.60E-04	6.4
221563_at	DUSP10	Bad	720	12	5.70E-04	1.05E-02	2.8	444	12	5.30E-04	1.9	401.1	3.9	4.80E-02	3.6
222631_at	PI4K2B	Bad	3375	15	1.20E-04	3.97E-03	4	2661	4.6	3.10E-02	1.7	1704.4	4.2	4.20E-02	4.4

Supplementary Table S3: 135 kinases differentially expressed in HM and HMCLs, identified with SAM (Significance Anlaysis of Microarray) methods

PROBESETS	Name	Score	Numerator	Denominator	Fold.Change	q.value...
1007_s_at	DDR1	-5.56966509	-496.5	89.14360048	0.376256281	0.00000000
1552504_a_at	BRSK1	-2.97655697	-146.254969	49.13561912	0.446288984	0.0000654
1552519_at	ACVR1C	-7.12091262	-515.683541	72.41818126	0.29226171	0.00000000
1553292_s_at	FLJ25006	4.341318031	185.1202034	42.64147481	2.044759374	0.00000000
201037_at	PFKP	15.17515524	5376.313222	354.2839027	29.10323844	0.00000000
201041_s_at	DUSP1	-15.1727110	-31113.273	2050.60736	0.037056265	0.00000000
201251_at	PKM2	14.48613457	4445.045307	306.8482683	7.648075545	0.00000000
201577_at	NME1	12.51857525	11905.36107	951.0156574	2.427579436	0.00000000
201897_s_at	CKS1B	24.94359149	11947.00046	478.9607169	7.652094611	0.00000000
202009_at	TWF2	8.598710763	536.4960703	62.39261735	2.196317361	0.00000000
202240_at	PLK1	17.69607521	849.5434582	48.00745071	5.549863571	0.00000000
202241_at	TRIB1	-12.4451630	-19472.9986	1564.704175	0.393618174	0.00000000
202545_at	PRKCD	-5.64289410	-718.366620	127.3046432	0.453816426	0.00000000
202686_s_at	AXL	-2.96179914	-157.694174	53.2426971	0.256840227	0.0000654
202786_at	STK39	8.279835751	1074.57767	129.7824863	2.873972487	0.00000000
202847_at	PCK2	6.191802676	1826.31484	294.9568867	2.062755772	0.00000000
202934_at	HK2	11.61746394	3420.087841	294.3919481	3.702797005	0.00000000
203027_s_at	MVD	3.071070261	105.3291724	34.29722003	2.30489593	0.0000626
203060_s_at	PAPSS2	-2.92385339	-548.908229	187.7345255	0.375127266	0.0000654
203104_at	CSF1R	-2.62413384	-151.171289	57.60807148	0.37851669	0.000121659
203302_at	DCK	16.63681248	2857.812067	171.7764187	6.017080864	0.00000000
203336_s_at	ITGB1BP1	15.13076717	2425.537679	160.3050032	3.145028363	0.00000000
203515_s_at	PMVK	8.886098547	3451.025428	388.3622727	2.460031501	0.00000000
203680_at	PRKAR2B	4.624439533	316.7041147	68.48486447	2.476242196	0.00000000
203755_at	BUB1B	28.24346508	7501.366158	265.5965243	10.92537368	0.00000000
203839_s_at	TNK2	-3.46119429	-187.509939	54.17492452	0.494952438	0.00000000
203856_at	VRK1	12.0280441	2185.171059	181.6730169	2.435705112	0.00000000
203942_s_at	MARK2	4.710268687	118.4260287	25.14209624	2.288871614	0.00000000
204061_at	PRKX	10.72195167	890.2515025	83.03073266	3.715869584	0.00000000
204106_at	TESK1	-6.03628995	-340.514563	56.4112337	0.474931509	0.00000000
204159_at	CDKN2C	10.5422295	5525.239482	524.1054068	5.674771471	0.00000000
204170_s_at	CKS2	10.89898969	7617.707582	698.9370392	3.000920306	0.00000000
204244_s_at	DBF4	10.14468794	2441.637309	240.681362	2.109184119	0.00000000
204252_at	CDK2	15.44691216	1523.617198	98.63571327	3.815792644	0.00000000
204267_x_at	PKMYT1	13.77404547	784.1546463	56.92987207	2.751787806	0.00000000
204276_at	TK2	-6.24682392	-497.859454	79.69801306	0.443185817	0.00000000
204396_s_at	GRK5	-4.39580676	-696.202496	158.3787764	0.464307592	0.00000000
204510_at	CDC7	15.37380505	1102.711512	71.72664855	4.261055032	0.00000000
204589_at	NUAK1	3.200300216	433.3326399	135.4037467	2.989713887	0.0000626
204632_at	RPS6KA4	-4.78924228	-296.405686	61.8898918	0.332492605	0.00000000
204641_at	NEK2	18.25192582	2725.442903	149.3235799	9.35391013	0.00000000
204718_at	EPHB6	-3.0981814	-107.459315	34.68464299	0.463679732	0.0000341
204794_at	DUSP2	-3.17685780	-2293.81715	722.0396032	0.280517917	0.0000341
204813_at	MAPK10	-5.64990500	-322.620896	57.10200376	0.37122836	0.00000000
204822_at	TTK	15.72079921	807.7632917	51.38182106	5.489389939	0.00000000
204825_at	MELK	26.28098502	8426.988442	320.6496422	7.955217212	0.00000000
204887_s_at	PLK4	16.09405341	916.5300509	56.94836641	5.763116892	0.00000000
204891_s_at	LCK	-2.84467946	-74.2004160	26.08392865	0.204471442	0.0000654
205050_s_at	MAPK8IP2	-4.72772400	-310.494452	65.67524913	0.176863044	0.00000000
205051_s_at	KIT	-3.22108301	-1524.90846	473.414828	0.23069673	0.00000000
205295_at	CKMT2	-3.04313912	-77.6886269	25.52910784	0.335443188	0.0000654
205394_at	CHEK1	16.69885918	1812.544152	108.5429928	5.566384102	0.00000000
205399_at	DCLK1	-2.73477029	-1185.76814	433.5896685	0.122353827	0.000121659
205406_s_at	SPA17	4.921174083	153.4736477	31.18638868	2.097153367	0.00000000
205418_at	FES	2.884083912	97.41146556	33.775531	2.0657936	0.000117659
205486_at	TESK2	-8.41394874	-719.453305	85.50721277	0.336633376	0.00000000
205504_at	BTK	-6.51913408	-942.784789	144.6181007	0.419092428	0.00000000
205578_at	ROR2	-3.82868808	-245.147480	64.02910731	0.350159809	0.00000000
205651_x_at	RAPGEF4	-3.26523213	-395.911696	121.2507044	0.408967117	0.00000000
205771_s_at	AKAP7	-8.88873206	-825.940822	92.91998194	0.286378372	0.00000000
205977_s_at	EPHA1	-3.34942192	-121.019648	36.13150312	0.423115871	0.00000000
205986_at	AATK	-4.00195772	-153.742025	38.41670396	0.359291595	0.00000000
206070_s_at	EPHA3	5.364543238	271.9831253	50.70014598	7.379201162	0.00000000
206170_at	ADRB2	-3.95839045	-1215.50878	307.0714717	0.411934387	0.00000000
206186_at	MPP3	-4.14100209	-195.699722	47.2590253	0.319270831	0.00000000
206271_at	TLR3	-3.30904069	-158.195099	47.80693674	0.177107457	0.00000000
206412_at	FER	2.252787768	372.6306056	165.4086599	2.031094668	0.000632132
206674_at	FLT3	-3.43442331	-226.946139	66.07983898	0.227870371	0.00000000

207106_s_at	LTK	-4.70158860	-243.626907	51.81799756	0.230034169	0.00000000
207541_s_at	EXOSC10	11.18229003	845.2773925	75.59072339	2.102866263	0.00000000
207655_s_at	BLNK	-8.91556109	-4731.59893	530.7124122	0.155025473	0.00000000
208018_s_at	HCK	-3.27771891	-229.653721	70.06510556	0.303700651	0.00000000
208078_s_at	SNF1LK	-9.86206320	-16095.4396	1632.056025	0.095613585	0.00000000
208079_s_at	AURKA	28.59732847	5577.573971	195.0382875	17.27934992	0.00000000
208260_at	AVPR1B	5.697288402	171.3280166	30.07185253	2.980004007	0.00000000
208892_s_at	DUSP6	-4.00433951	-2079.34512	519.2729319	0.433169029	0.00000000
208932_at	PPP4C	16.6804997	2276.635691	136.4848615	3.734282988	0.00000000
209018_s_at	PINK1	-6.39018347	-755.104022	118.1662507	0.478505335	0.00000000
209457_at	DUSP5	-5.42096159	-5195.31137	958.374503	0.475967269	0.00000000
209464_at	AURKB	15.16052728	643.8395747	42.46815186	4.670225873	0.00000000
209642_at	BUB1	25.48323633	3445.744799	135.216138	10.48201214	0.00000000
209685_s_at	PRKCB	-5.59886004	-2625.44752	468.925372	0.210509289	0.00000000
209825_s_at	UCK2	15.92105613	3291.103098	206.7138681	3.603540826	0.00000000
210001_s_at	SOCS1	-3.16195787	-207.469949	65.61439378	0.374944286	0.0000341
210176_at	TLR1	-8.22431410	-910.163892	110.6674527	0.140019714	0.00000000
210416_s_at	CHEK2	13.16981253	926.827092	70.3751166	3.310841918	0.00000000
211339_s_at	ITK	-3.46864791	-93.0871474	26.8367242	0.382814536	0.00000000
211432_s_at	TYRO3	5.696533579	273.4271845	47.99887171	2.702823629	0.00000000
212629_s_at	PKN2	-6.54869549	-1127.5319	172.1765658	0.465288852	0.00000000
213076_at	ITPKC	-3.75014645	-257.743874	68.72901565	0.471352522	0.00000000
213093_at	PRKCA	-6.59377071	-1367.90545	207.454204	0.15025655	0.00000000
213107_at	TNIK	2.731808479	198.2815534	72.5825236	2.088153022	0.000174456
213178_s_at	MAPK8IP3	-3.06931196	-321.766990	104.8335894	0.407718496	0.0000341
213324_at	SRC	-2.91090543	-322.602172	110.8253702	0.315598731	0.0000654
213348_at	CDKN1C	-3.24214017	-439.377022	135.5206742	0.415755987	0.00000000
214464_at	CDC42BPA	4.594081309	392.278086	85.38771076	4.421512648	0.00000000
214575_s_at	AZU1	-2.79515319	-79.4676375	28.43051241	0.238093022	0.000121659
214607_at	PAK3	-3.71874117	-138.447757	37.22973752	0.167268005	0.00000000
214683_s_at	CLK1	-5.90724754	-2768.17244	468.6061361	0.318193094	0.00000000
216199_s_at	MAP3K4	9.944026322	1010.876791	101.656689	2.189660876	0.00000000
217147_s_at	TRAT1	-2.91598495	-667.828479	229.0232938	0.222999126	0.0000654
217149_x_at	TNK1	-5.01834535	-488.832177	97.40903487	0.302852791	0.00000000
218145_at	TRIB3	8.438637513	2437.686546	288.8720534	3.0264132	0.00000000
218311_at	MAP4K3	-6.06409781	-972.836800	160.4256447	0.435195828	0.00000000
218499_at	RP6-213H19.	11.90886526	5844.716366	490.7870095	2.348996297	0.00000000
218696_at	EIF2AK3	-8.42425131	-7442.68677	883.4834693	0.411263954	0.00000000
219148_at	PBK	18.97233726	3301.265141	174.0041354	11.672305	0.00000000
219365_s_at	CAMKV	-2.87532559	-109.391123	38.04477781	0.416686389	0.0000654
219686_at	STK32B	2.182895895	66.57235321	30.49726437	2.211475686	0.000632132
221215_s_at	RIPK4	-3.06214078	-85.0968562	27.78998814	0.318325075	0.0000654
222164_at	FGFR1	-3.24115814	-220.478502	68.02460478	0.443406681	0.00000000
223551_at	PKIB	2.336934369	141.5758206	60.58185565	2.252668115	0.000518886
224823_at	MYLK	4.645778396	1175.242256	252.9699344	2.887085849	0.00000000
224851_at	CDK6	12.43058357	3394.847896	273.1044668	4.453609554	0.00000000
225164_s_at	EIF2AK4	-8.15979659	-1970.07558	241.4368503	0.355282359	0.00000000
225207_at	PDK4	-3.18996778	-906.167591	284.0679448	0.025153019	0.0000341
225330_at	IGF1R	5.898392815	417.3950532	70.76420073	2.215089538	0.00000000
225342_at	AK3L1	7.519679488	1019.727462	135.6078359	4.660733268	0.00000000
226101_at	PRKCE	-4.10010025	-236.779473	57.74967891	0.227277356	0.00000000
226605_at	DGKQ	-4.67961624	-340.284558	72.7163384	0.382075254	0.00000000
226649_at	PANK1	7.407447875	412.5175682	55.68956747	2.633230556	0.00000000
227053_at	PACSIN1	5.828365628	684.616736	117.4629012	3.474923621	0.00000000
227266_s_at	FYB	-2.61184985	-113.361072	43.40259929	0.163117082	0.000121659
227750_at	KALRN	-3.8833956	-193.209431	49.75270389	0.331444025	0.00000000
227767_at	CSNK1G3	-9.52919969	-1988.8546	208.711609	0.282808855	0.00000000
228139_at	RIPK3	-6.84686700	-284.889967	41.60880698	0.333159107	0.00000000
228367_at	ALPK2	3.299466156	400.9519186	121.5202398	4.660849891	0.0000341
228499_at	PFKFB4	7.670548531	713.605178	93.03183145	4.528713283	0.00000000
228565_at	KIAA1804	7.564448471	909.7905687	120.2718972	2.367088212	0.00000000
230425_at	EPHB1	-3.37079767	-646.423717	191.7717348	0.221171689	0.00000000
231775_at	TNFRSF10A	7.583292108	863.6266759	113.8854555	2.060511071	0.00000000
235085_at	PRAGMIN	3.356562247	179.0811373	53.3525447	2.020461793	0.00000000
236313_at	CDKN2B	3.804243087	110.0397596	28.92553317	2.343379784	0.00000000
238025_at	MLKL	-6.79985473	-1496.53166	220.0828881	0.280310385	0.00000000
38269_at	PRKD2	-7.33645253	-5443.75774	742.0149881	0.455394487	0.00000000