damage is Poly(ADP-ribose) polymerase 1 (PARP1) recruitment which is a sensor for single strand breaks in DNA. PARP1 catalyzes the synthesis of poly(ADP-ribose) or PAR which is needed for the recruitment of many other DNA repair proteins by means of PAR-binding domains.

We used high speed confocal spinning-disk microscopy of living cells to obtain precise kinetics of recruitment of PAR-dependent proteins to the sites of laser induced DNA damage.

Our results show that the investigated PAR-dependent proteins are recruited to DNA damage sites in the matter of seconds, they reach peak intensities for 20 to 30 seconds after damage infliction and start dissociating. The recruitment of the proteins is entirely dependent on PAR because addition of PARP inhibitor abbrogated their recruitment.

The use of spinning-disk microscopy of living cells allowed us to obtain the kinetics of recruitment of the studied proteins to the sites of DNA damage. The results are consistent with the fact that PARP1 and PAR-dependent proteins are quickly recruited to damage sites and generation of PAR is essential for other DNA repair protein recruitment. The precise kinetic curves may serve as a basis for investigating how they will change or if they will change at all when cells are put in different conditions or treated with various chemical substances affecting DNA metabolism and repair.

## P-05.01.1-035
## A benzamide derivative XT5 and imatinib combination induced apoptosis in İmatinib resistant K562 cell line

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**Introduction:** Chronic myeloid leukemia (CML) is a myeloproliferative disease associated with reciprocal translocation between chromosomes 9 and 22. BCR-ABL fusion gene which exhibits constitutively active tyrosine kinase activity has a main role in CML. The tyrosine kinase inhibitor imatinib is used as a first line treatment in CML patients, but imatinib resistance leads to failure in therapy. The application of imatinib in combination with other anticancer agents may be a strategy to increase the antileukemic effect of imatinib. In this study, we have investigated the antiproliferative effect two novel agents: a benzamide derivative XT5 and a benzoxazole derivative XT2B in combination with imatinib. These molecules were investigated in imatinib-sensitive (K562s) and imatinib-resistant (K562r) CML cell lines.
**Materials and Methods:** Antiproliferative and apoptotic effects were assessed by MTT assays and flow-cytometry, respectively. We also evaluated the effects of these compounds on the expression of apoptosis-related genes BAX, BCL-2, BAD, BIM, BCL-XL and MCL1 by real-time quantitative PCR.
**Results:** Treatment of K562 cells with XT5 increased the expression levels of the pro-apoptotic genes BAX, BAD and BIM in both sensitive and resistant cells. However, XT2B was not found to have similar effects on K562r and K562s cells. Combined application of XT5 increased cell death in the MTT assay. MTT assay demonstrated that IC50 for XT5 treated cells in K562r with imatinib (IC50 = 3.5) is lower than K562r without imatinib (IC50 = 8.5).
**Discussion and Conclusion:** Our results showed that combining XT5 with imatinib has more antiproliferative and apoptotic effect on a CML cell line. As a result combination of XT5 with imatinib can be an alternative approach to overcome imatinib resistance.

## P-05.01.1-036
## Effects of MLH1 and MSH2 expression on imatinib resistance in CML

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**Introduction:** The MMR(Mismatche Repair) system recognizes base–base mismatches and insertion or deletion loops in double-stranded DNA, and it degrades the error-containing region of the newly synthesized strand, allowing the polymerase to correctly resynthesize the second strand according to the template sequence. The human MMR system includes the MLH1 and MSH2. Alteration in expression or a defect in MLH1 or MSH2 can cause resistance to anti-cancer drugs used in chemotherapy. The attempt of the MMR system to detect drug induced DNA damage, triggers the activation of apoptosis, a mechanism which may enhance the cytotoxicity of chemotherapy. Loss of the MMR system would make the neoplastic cell less able to initiate apoptosis. Inability to initiate apoptosis could be a mechanism of resistance to drugs. Chronic myeloid leukemia (CML) is a clonal disease originating from aberrations in hematopoietic stem cell. Imatinib, a tyrosine kinase inhibitor has significantly improved clinical outcome for CML patients. However, patients develop resistance when the disease progresses to the blast phase (BP) and there are several mechanisms involved in imatinib resistance. In this study we investigated the role of MMR system in imatinib resistance.
**Materials and Methods:** K562s (sensitive) and K562r (resistance) were grown in RPMI-1640. K562r cells were maintained in RPMI-1640 medium supplemented with 5 μM imatinib RNA isolation, cDNA synthesis, RT- PCR was performed respectively.
**Results:** The results demonstrated that expression of MLH1 in K562r cells is dramatically lower than equal amount of imatinib treated K562s cells, whereas MSH2 expression level did not change in both cell lines.
**Conclusion:** It can be suggested that alteration and down-regulation of MLH1 genes leads to imatinib resistance.

## P-05.01.1-037
## Characterization of interaction between Rad51 inhibitor DIDS and human serum albumin

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4′-diisothiocyanostilbene-2,2′-disulfonic acid (DIDS) has been largely used during the last 30 years for its inhibitory effect on anion transporters and channels. More recently, Ishida and colleagues have described a possible mechanism by which DIDS inhibits Rad51-mediated homologous pairing and strand exchange, key processes in DNA repair by Homologous Recombination. Thus, DIDS could act as a potential revertant of radio- and chemo-resistance in cancer cells, which is the major cause of failure during therapeutic protocols. New drugs targeting Rad51 protein have since been developed with potential use for medical applications. In this context, we attempted to determine the behaviour of DIDS towards blood and plasma proteins such as serum albumins. Firstly, we analysed the effects of several environmental factors such as solvent polarity, which may affect the stability of the molecule. Secondly, we analysed the spectroscopic properties of DIDS in the presence of Human or Bovine Serum


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