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**Presentation Title:** Synthesis and biological evaluation of new purine-like heterocyclic molecules targeting apoptosis in cancer cell lines
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**Abstract:**

Chemotherapy remains its position on the frontline of leukaemia treatment. Many of the modern antileukaemic drugs are purine analogues, e.g. pentostatin, cladribine, and fludarabine. In our program on the development of new potent antiproliferative agents selectively targeting leukaemic cells, we identified a new type of purine-like compounds possessing the desirable properties. We prepared a representative library of these compounds and preliminary screening identified several potent molecules, including compound MM0018. Its anti-proliferative activity against Jurkat T cells was assessed at wide range of concentrations and three time points (24, 48, and 72 h). MM0018 demonstrated significant and concentration dependent inhibition of the Jurkat T cell growth with $GI_{50}$ values of 50.0 ± 0.2 ng/mL, 7.60 ± 0.4 ng/mL and 1.30 ± 0.1 ng/mL ($p < 0.05$) at these points, respectively. The effect of the compounds on the cell morphology was studied microscopically using Hoechst fluorescence staining and acridine orange and propidium iodide (AO/Pi) immunohistochemical staining. It was found that Jurkat T cells treated with $GI_{20}$ and $GI_{50}$ of MM0018 at two time points (24 and 48 h) demonstrated hallmarks of apoptosis, such as chromatin condensation, multi-nucleated cells, and formation of apoptotic bodies. It showed that this compound activated caspases-dependent apoptosis pathway as apoptosis was inhibited when caspases-inhibitor z-VAD-fmk was added. No effects on the proliferation of lung cancer (A549), nasopharyngeal carcinoma (HKL), and non-cancerous human lung fibroblast (MRC-5) cells were observed when they were treated with MM0018 at concentrations up to 300 ng/mL. Therefore, we can conclude that MM0018, due to its high potency and selectivity, has a potential for the further development as an apoptosis-inducing antileukaemic agent.