# Med Chem Seminar

**Wednesday 13 November , 13.00 – 14, Auditorium 1, School of Pharmacy, The University of Oslo**

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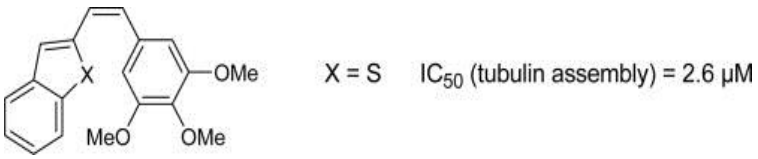
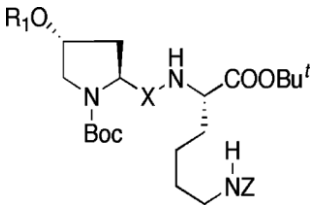
### Fighting cancer with small molecules: design of new cytotoxic agents and chemosensitizers.

The first part of the Conference will present a novel series of combretastatin A-4 heterocyclic analogues. Target compounds were prepared by replacement of the B ring with indole, benzofurane or benzothiophene, attached at the C2 position. These compounds were evaluated for their abilities to inhibit tubulin assembly: derivative **cis3b**, having a benzothiophene, showed an activity similar to those of colchicine or deoxypodophyllotoxine. The antiproliferative and antimitotic properties of **cis3b** against keratinocyte cancer cell lines were also evaluated and the intracellular organization of microtubules in the cells after treatment with both stereoisomers of **3b** was also determined, using confocal microscopy.

A: compound **3b**




B: Reversin **121**




The second part of the Conference will present a novel class of P-gp/ABCB1 ligands, known as reversins. N$^{a}$-Boc-L-Asp(OBn)-L-Lys(Z)-OtBu (reversin 121), an inhibitor of the P-gp ABC transporter, was used to conceive our compounds inhibiting the drug efflux occurring through the Hoechst 33342 and daunorubicin transport sites of P-gp, respectively Hand R sites. ABC (ATP-binding cassette) transporters are involved in several genetic diseases and are responsible for the cellular multidrug resistance phenotype encountered during chemotherapeutic treatments against cancer and viral diseases. In such a context, they represent a serious threat, since cancer cells overexpress them to reduce drug concentration below its cytotoxic threshold. The most potent compound behaved as a noncompetitive inhibitor for both the R and H drug-transport sites of P-gp, which limits the possibility for such an inhibitor to be itself transported by P-gp.

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