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FAKULTET: Det matematisk-naturvitenskapelige fakultet
INSTITUTT: Farmasøytisk
FAGOMRÅDE: Farmakologi og toksikologi
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AVHANDLINGENS TITTEL: *Mechanism of cell death induced by caspase activators PAC-1 and 1541 and tubulin inhibitor combrestastatin A-4*
Crosstalk between caspases, ROS and growth factors

Cancer is one of the most important diseases in human history. To find out proper remedy to cure this disease is challenge. There are many checkpoints in the cell which are important to understand before finding a therapeutic agent. Caspase -3, ROS and tublin inhibition are interesting target in this context. PAC-1 was discovered as anticancer and direct activator of caspase-3 in 2006, and later in 2009 1541 was also presented as direct activator of caspase-3. Combrestatin A-4 was introduced as tublin inhibitor, but is also caspase-3 activator and ROS producer. It was interesting to study these anticancer drugs in Cerebellar granule neurons (CGN) and PC12 cell (a pheochromocytoma cell line) and explore the detailed mechanisms of these potential anticancer drugs.

PhD candidate Gulzeb Aziz M.Phil (Pharmacy) has worked with PAC-1, 1541, CA-4 and its triazole analogues in CGN and PC12 cells. These anticancer drugs were synthesized in collaboration with Trond V.Hansen and then biologically tested. This study will shed light on potential neurotoxicity of these compounds and may contribute to the understanding of caspase-3 function in neurons. This study shed light on the detailed mechanisms involved in the cell death induced by CA-4 and its triazole analogues.

The PhD work was carried out in January 2008 to September 2011 in the department of Pharmaceutical Biosciences, School of Pharmacy, University of Oslo in the subject of Pharmacology and toxicology. Professor Ragnhild E. Paulsen is main supervisor and Professor Tor Gjøen and Associate Professor Trond V. Hansen are co-supervisors.