



UNIVERSITY OF GOTHENBURG  
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**Abstract** - Master Thesis Project, the Pharmacy Programme

## **TNF- $\alpha$ -induced NADPH oxidase activity in human polymorphonuclear leukocytes**

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Binding of TNF $\alpha$  to PMN receptor triggers an activation of the NADPH oxidase, the result being a metabolic burst and generation highly-reactive oxygen species (ROS). Uniquely the activating signals are generated exclusively in adherent PMN. The plasma level of TNF $\alpha$  is high in Rheumatoid Arthritis (RA). Thus, anti-TNF $\alpha$  therapy is now increasingly used to treat RA-patients. Unfortunately, this treatment does not work in all patients. The aim of this master thesis was to set up a technique to measure PMN production of ROS in response to TNF $\alpha$ -simulation. As mentioned, previous studies have shown that PMN cells cannot be activated by TNF $\alpha$  when the cells are in suspension. The intentions were to use the established technique to determine the response by cells isolated from patients with RA, and investigate if the activity could be used to predict if new patients would turn out as responders or non-responders in relation to anti-TNF-treatment.

The H<sub>2</sub>O<sub>2</sub> production from PMNs, adherent to a polystyrene surface coated with FCS could be measured by a hydrogen peroxide fluorometry technique. It was also possible to follow ROS production by the chemiluminescence technique designed to measure O<sub>2</sub><sup>-</sup> production.

TNF $\alpha$ -induced ROS produces both at the plasma-membrane and in intracellular-organelles.

In conclusion, a technique was established that can be used to measure TNF $\alpha$ -induced ROS production in PMN, and the basic characteristics of this response was determined. Due to lack of time, it was not possible to initiate the part of the project that involved cells from patients suffering from RA.