

## Persistent Inflammation in HIV Infection

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Linn Landrø defended her PhD thesis on February 16, 2012 at the University of Oslo. Her main supervisors were Stig Frøland and Pål Aukrust, both at the Department of Clinical Immunology and Infectious Diseases, Oslo University Hospital, and Jan Kristian Damås, Centre of Molecular Inflammation Research, NTNU, Trondheim. Members of the evaluation committee were Anne Ma Dyrhol-Riise, Oslo (1<sup>st</sup> opponent), Anders Waage, Trondheim (2<sup>nd</sup> opponent) and Britt Nakstad, Oslo. Dr Landrø is presently at the Department of Dermatology, Oslo University Hospital, Rikshospitalet, Oslo, Norway.

Since it was first isolated in 1983, the human immunodeficiency virus (HIV) has been one of the leading causes of death by infectious agents worldwide. HIV invades the immune system and causes a progressive immune deficiency which ultimately is fatal. The pathogenesis of HIV-induced immune deficiency is complex and involves both the innate and the adaptive immune system. Following primary infection, there is an acute immune response with a substantial loss of CD4+ T cells. In the chronic phase, which can last from 6 to 15 years, there is a gradual CD4+ T-cell depletion which finally will result in a profound immune deficiency, placing the patient at risk of developing infections and malignancies.

Antiretroviral therapy against HIV has dramatically changed the outcome of the disease. Treatment with a triple combination therapy will usually result in restoration of several immune functions. However, despite of viral suppression, there seems to be a low-grade systemic immune activation and inflammation indicating that the medications are not able to correct all aspects of the immune system.

The aim of this thesis was to explore the character and role of innate immune responses and inflammation in the persistent immune activation in HIV infection by both *in vivo* and *in vitro* analysis. The group were able to show that this persistent immune activation and inflammation involve homeostatic chemokines, CXCL16 and platelet-derived inflammatory mediators. These mediators can be part of a pathogenic loop promoting HIV replication and inflammation even during apparently successful antiretroviral treatment. In addition to

promoting HIV replication and immunodeficiency, this persistent inflammation could contribute to the increased occurrence of cardiovascular and metabolic disorders that are seen in HIV-infected patients also during apparently successful antiretroviral treatment.



### List of papers

1. Landrø L, Damås JK, Flo TH, Heggelund L, Ueland T, Tjønnfjord GE, et al. Decreased serum lipocalin-2 levels in human immunodeficiency virus-infected patients: increase during highly active anti-retroviral therapy. *Clin Exp Immunol* 2008; 152: 57–63.
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3. Damås JK, Landrø L, Fevang B, Heggelund L, Frøland SS, Aukrust P. Enhanced levels of the CCR7 ligands CCL19 and CCL21 in HIV infection: correlation with viral load, disease progression and response to highly active antiretroviral therapy. *AIDS* 2009; 23: 135–138.
4. Damås JK, Landrø L, Fevang B, Heggelund L, Tjønnfjord GE, Fløisand Y, et al Homeostatic chemokines CCL19 and CCL21 promote inflammation in human immunodeficiency virus-infected patients with ongoing viral replication. *Clin Exp Immunol* 2009; 157: 400–407.
5. Landrø L, Ueland T, Otterdal K, Frøland SS, Aukrust P. Persistently raised plasma levels of platelet-derived inflammatory mediators in HIV-infected patients during highly active anti-retroviral therapy. *J Thromb Haemost* 2011; 9: 1075–1077.