HIV persistence and viral reservoirs

Although antiretroviral treatment (ART) has substantially improved the prognosis for HIV-infected patients, it does not cure the infection. Replication-competent HIV-1 persists in stable reservoirs, such as in resting CD4+ T-lymphocytes and in cells within the central nervous system (CNS). Those reservoirs enable long-term persistence of the infection during otherwise effective ART. HIV infects the CNS early in the infectious course and establishes a chronic brain infection. Neurocognitive dysfunction is a frequent complication and 20-50% of HIV-infected patients have signs of neurocognitive disorders despite effective ART.

This research program is based on 3 closely linked sections reflecting separate areas of HIV persistence.

1. HIV infection of the CNS.
Aims: To study the pathogenesis of HIV CNS disease, find prognostic and diagnostic markers of AIDS dementia, and to study effects of treatment on the CNS infection.
Study plan: A cohort from 4 sites; Gothenburg, San Francisco, Sydney, and Milan, will be followed, and studied longitudinally and crossectionally with focus on cerebrospinal fluid (CSF) markers.
Importance: The pathogenesis of HIV-related CNS dysfunction is still largely unexplained. This study may shed light on pathogenic mechanisms and also propose prognostic and diagnostic markers.

2. The CNS as an HIV reservoir during ART.
Aims: To study the HIV CNS infection during effective ART and characterize the CSF residual viremia and immunoactivation.
Study plan: Crossectional and longitudinal genotypic characterizations of residual viremia in CSF as compared to blood are performed in collaboration with sites in San Francisco and Stockholm. Treatment intensification studies ongoing to settle if viremia and immunoactivation is a result of residual replication or release from stable reservoirs.
Importance: Characterization of the CNS HIV reservoir is important both for understanding of pathogenic mechanism behind neurocognitive disorders and to find methods to purge this reservoir.

3. New approaches to resist the hidden reservoirs of HIV.
Aims: To explore approaches to activate resting CD4+ T-cells and thereby making this infection susceptible to ART.
Study plan: Studies looking at different aspects of viral latency are ongoing.
Importance: Finding mechanisms to reach HIV in reservoirs are essential if HIV-infection ever will be possible to cure.

Ten important publications of last three years:


4. Edén A, Price RW, Spudich S, Fuchs D, Hagberg L, Gisslén M. Central nervous system immune activation is still present after more than four years of effective HAART. *J Infect Dis* 2007, 196:1779-1783


**Group members**

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CURRICULUM VITAE

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MD, June 1988

Residency (AT):
Kungälv Hospital, Kungälv, Departments of Internal Medicine, Surgery, Anaesthesiology, and Psychiatry.
1990-1992

Fellowship in infectious diseases (ST):
Mölndal Hospital, Göteborg, Department of Internal Medicine and Paediatrics.
1994-1995
Sahlgrenska University Hospital, Göteborg, Department of Virology.
1995
Östra University Hospital, Göteborg, Department of Infectious Diseases.

Board certification
Specialist in Infectious Diseases, March 3, 1997

Present positions
Senior consultant, Assoc. Professor, Department of Infectious Diseases, Sahlgrenska University Hospital, Gothenburg, Sweden, 2003-present

Team chief of the HIV section at the Department of Infectious Diseases, Sahlgrenska University Hospital, Gothenburg, Sweden, 2000-present

Research position (50%) in Clinical HIV Research at the Swedish Research Council, 2008-present

HIV consultant at 18 Hospitals in Sweden

Scientific experiences
Thesis, University of Gothenburg, 1996 (Cerebrospinal fluid markers of HIV-1 infection and effects of antiviral treatment)
Associate Professor (Docent), University of Gothenburg, 1999

Scientific publications, presently >70 titles.

Editorial board for:
AIDS Research and Therapy, BMC (section editor), 2006-present
The Open AIDS Journal, Bentham Science Publishers, 2007-present
AIDS Research and Treatment, Hindawi Publishing Corp, 2009-present
Neurobehavioral HIV Medicine, Dove Medical Press, 2009-present


Participation in several national and international scientific advisory boards (HIV)

Appointed for The Swedish National Board of Health and Welfare as expert on HIV
Member of NIMH/NINDS Consensus Meeting (US National Institute of Health, NIH) for update on diagnostic definitions of HIV-associated dementia and minor cognitive motor disorder in the era of HAART 2005 (Published guidelines, Neurology, 2007).
Member in steering committee of the Nordic HIV Clinical Research Network.
Founder of and steering committee member of the Swedish National HIV Register – InfCare HIV
Member of the steering committee/faculty of HIV and the brain (HIV and the Body), 2010

Participated with speeches, posters and as moderator/chairmen at a large number of national and international scientific meetings

**Supervisor, PhD-degree:**
Lars-Magnus Andersson, MD, dissertation January 24, 2003
Sahra Abdulle, MD, dissertation June 16, 2006
Åsa Mellgren, MD, dissertation December 15, 2006
Aylin Yilmaz, MD, dissertation June 14, 2007
Arvid Edén, MD, dissertation June 18, 2010
Eva-Corina Caragounis, MD, Jan Krut, MD, Arash Izadkhasti, MD, Tomas Mellberg, MD, Helena Abrahamsson, MD

**Scientific prices**
Junior Scholarship Award (3rd International Congress on Drug Therapy in HIV Infection, Birmingham, UK), 1996

The Domagk Price, 2003

Gothenburg, May 14, 2010

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