

Aspects of infection and leukemia in Rwanda

Akademisk avhandling

som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien, Göteborgs universitet,
kommer att offentligens försvaras

tisdagen den 9 juni 2020 klockan 13.00 i föreläsningssal Gösta Sandels, Medicinargatan 9B, Göteborg

av

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Avhandlingen baseras på följande arbeten:

- I. **Belson Rugwizangoga***, Maria E. Andersson *, Jean-Claude Kabayiza, Malin S. Nilsson, Brynja Ármannsdóttir, Johan Aurelius, Staffan Nilsson, Kristoffer Hellstrand, Magnus Lindh, Anna Martner.
IFNLA genotypes predict clearance of RNA viruses in Rwandan children with upper respiratory tract infections.
Front. Cell. Infect. Microbiol. 2019;9:340. doi: 10.3389/fcimb.2019.00340.
*Equal contribution
- II. **Belson Rugwizangoga**, Anna Rydström, Johan Aurelius, Egide Kayitare, Fabien Ntaganda, Ka-Wei Tang, Kristoffer Hellstrand, Anna Martner.
Incidence, subtypes and outcome of acute myeloid leukemia in Rwanda.
In Manuscript.
- III. **Belson Rugwizangoga**, Anna Rydström, Johan Aurelius, Egide Kayitare, Fabien Ntaganda, Ka-Wei Tang, Kristoffer Hellstrand, Anna Martner.
Aspects of incidence, subtypes, and outcome of acute lymphoblastic leukemia in the Rwandan population.
In Manuscript.
- IV. **Belson Rugwizangoga***, Narcisse Niyikora*, Angèle Musabyimana*, Annie-Isabelle Izimukwiye, Johan Aurelius, Anna Martner, Aline Umubyeyi.
Experience and perception of acute leukemia in Rwanda by patients and healthcare professionals.
Submitted.
*Equal contribution

Disputationen kan följas digitalt (Zoom-id 633 2716 2136) och i föreläsningssal Ivan Östholm,
Medicinargatan 13C, Göteborg



UNIVERSITY OF GOTHENBURG

Aspects of infection and leukemia in Rwanda

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ABSTRACT

A first part of this thesis addressed the potential impact of variants of genes encoding interferon- λ 4, which is a cytokine that participates in protection against pathogens at epithelial surfaces, for the resolution of upper respiratory tract infections in Rwandan children. In a study of 480 subjects (≤ 5 years old), where follow-up samples were available from 161 subjects, it was observed that *IFNL4* genotypes were associated with clearance of RNA viruses from upper airways. Our results thus suggest that *IFNL4* variants that are overrepresented among subjects of African descent, such as TT at *rs12979860*, entail reduced clearance of respiratory RNA viruses, in particular ss(+)RNA viruses (**Paper I**). A second part aimed at determining the epidemiology, subtypes and outcome of acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML) in Rwanda using contemporary western world databases for comparison. In **Paper II**, which comprises observations made in 180 Rwandan AML cases diagnosed in 2012-17, we show that AML occurs less frequently and at a younger age in Rwanda than in Sweden. The outcome of AML in terms of survival is distinctively poor in Rwanda, which is likely explained by the shortage of AML therapy with curative intent and, possibly, by the accumulation of somatic gene aberrations that have been shown to predict poor prognosis for survival. Similarly, the results presented in **Paper III** imply that the incidence of ALL, based on a study comprising 318 Rwandan cases, was lower in Rwanda than in Sweden with a lower peak age at diagnosis. Although protocols for ALL treatment are available in Rwanda, the survival in ALL was clearly inferior to that of patients in the western world, in particular among children. We observed an apparent accumulation of T-ALL subtypes in Rwandan patients along with genomic abnormalities associated with poor survival outcome, including somatic mutations of *NOTCH1*. We also noted that serological signs of recent EBV infection and malaria, which have been associated with Burkitt leukemia/lymphoma in regions where malaria is holoendemic, were more common in ALL than in AML patients. Analysis of the genetic profile and morphology of Rwandan EBV/malaria-related ALL cases suggested the existence of a lymphoproliferative disorder distinct from Burkitt leukemia/lymphoma. In **Paper IV**, we investigated factors of potential relevance to the low incidence of and poor outcome of ALL and AML in Rwanda and identified the contribution by low awareness, financial constraints and an insufficiently efficacious referral system along with suboptimal diagnostic and treatment capacities. In conclusion, this work may spark further studies and interventions aiming to improve healthcare in Rwanda and similar developing countries.

Keywords: interferon- λ , respiratory infection, nucleotide polymorphism, acute leukemia, Rwanda, Epstein-Barr virus, malaria

ISBN 978-91-7833-894-8 (PRINT)

ISBN 978-91-7833-895-5 (PDF)

<http://hdl.handle.net/2077/63615>