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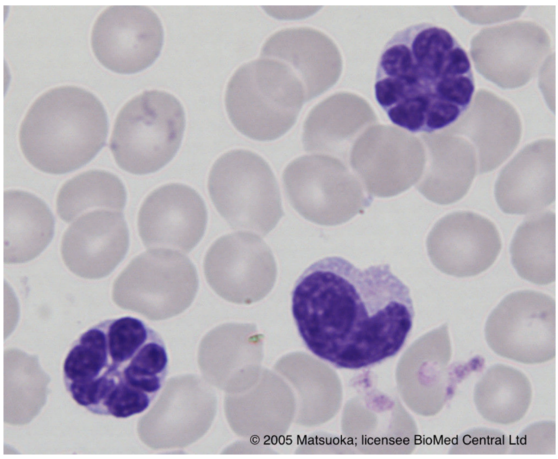
gesval s.a.

NGS MAPPING OF HTLV-1 INTEGRATION SITES: A TOOL TO IDENTIFY ASYMPTOMATIC CARRIERS AT HIGH RISK OF PROGRESSION TO AGGRESSIVE ATL



KEY ACHIEVEMENTS

- Set up of a NGS assay that, by targeting both the 3' and 5' viral LTRs, increases the dynamic range and number of integration sites retrieved.
- Pilot study showing that molecular characterization of HTLV-1 clonal architecture and follow up of the dominant malignant clone enables a more reliable definition of remission and a better estimate of molecular response in ATL patients.

KEY COMPETITIVE ADVANTAGES

- Detection of 5'deleted defective proviruses
- Ability to longitudinally monitor ATL patients
- Evaluation of therapeutic response
- Reduction of cost and hands-on time
- Integration in routine oncology sequencing program

UPCOMING CHALLENGES

The method is currently being further evaluated on a larger cohort of HTLV-1 infected individuals* at various stages of the disease (asymptomatic carriers, smoldering, chronic, acute ATL). This work will validate the clinical significance of the assay to (i) refine ATL subtypes and (ii) predict HTLV-1 carriers at high risk of progression to aggressive disease.

*in collaboration with the Japanese JSPFAD Biomaterial Bank (Joint Study on Predisposing Factors on ATL Development).

PARTNERSHIP SOUGHT

Companies developing molecular tools to follow HTLV-1 infection.

Human T-cell leukemia virus-1 (HTLV-1) is estimated to infect 20 million people worldwide with endemic regions involving Japan, the Caribbean area, Central and South America, West Africa, Central Australia, pockets in Europe and in the Middle East. HTLV-1 induces a very aggressive T-cell leukemia (adult T-cell leukemia, ATL) in addition to other diseases. It is commonly accepted that life-time risk of HTLV-1 infected people to develop ATL is about 5 %. However, a recent study suggests the risk among perinatally infected carriers may reach 25 %. Despite the development of new therapeutic approaches, ATL prognosis is still extremely poor. There is an urgent need for **molecular tools that integrate specific aspects of ATL/HTLV-1 physiopathology to (i) identify asymptomatic carriers at high risk of progression to ATL, (ii) more reliably evaluate therapeutic response and anticipate remission, and (iii) assist in the evaluation of clinical trials.**

The proviral integration site in the host genome is a main molecular attribute of HTLV-1. The development of ATL is associated with the emergence of a single predominant clone, with an underlying polyclonal population of infected cells. In the majority of ATL cases examined to date, the presumed malignant clone carries a single proviral integration. Improving the sensitivity and accuracy of clone abundance detection in tumors will undoubtedly improve patient classification and care at the asymptomatic and leukemic stages.

In this context, Anne Van den Broeke (GIGA-Medical Genomics, Université de Liège, Belgium) and collaborators developed a novel **NGS-based assay that identifies both 3' and 5'-LTR host junction sequences** (Leukemia, 2017, Volume 31, 2532–2535). This optimized method is **more sensitive, faster and cheaper** than existing protocols and **can be integrated within routine NGS programs used in a clinical setting.**

INTELLECTUAL PROPERTY

Monitoring method for adult T-cell leukemia/lymphoma (ATL) Patent application WO2018/184683

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