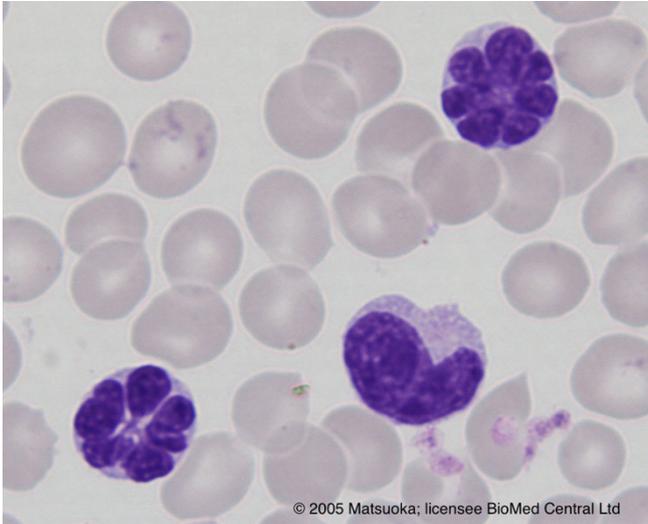


HTS MAPPING OF HTLV-1 INTEGRATION SITES: A TOOL TO MONITOR MOLECULAR RESPONSE IN ATL



KEY ACHIEVEMENTS

- Set up of a high throughput sequencing assay that, by targeting both 3'LTR and 5'LTR, increases the dynamic range and the number of integration sites retrieved
- Pilot study showing that molecular knowledge 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
- Ability to evaluate therapeutic response
- Reduction of hands-on time
- Reduction of costs
- In routine sequencing programs

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, smoldering, chronic, acute). 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.

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

T-cell leukemia virus-1 (HTLV-1) is estimated to infect 10 to 20 million people worldwide and shows an endemic distribution 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 reliably evaluate therapeutic response and better define remission.

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 dominant 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.

In this context, Anne Van den Broeke (GIGA-Medical Genomics, Université de Liège, Belgium) and collaborators developed a novel **sequencing-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 sequencing programs used in a clinical setting**.

PARTNERSHIP SOUGHT

- Companies developing molecular tools to classify ATL patients
- Companies developing ATL clinical studies

INTELLECTUAL PROPERTY

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

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