

CRYOSTEM : a French national Biobank to move research forward in the field of GvHD

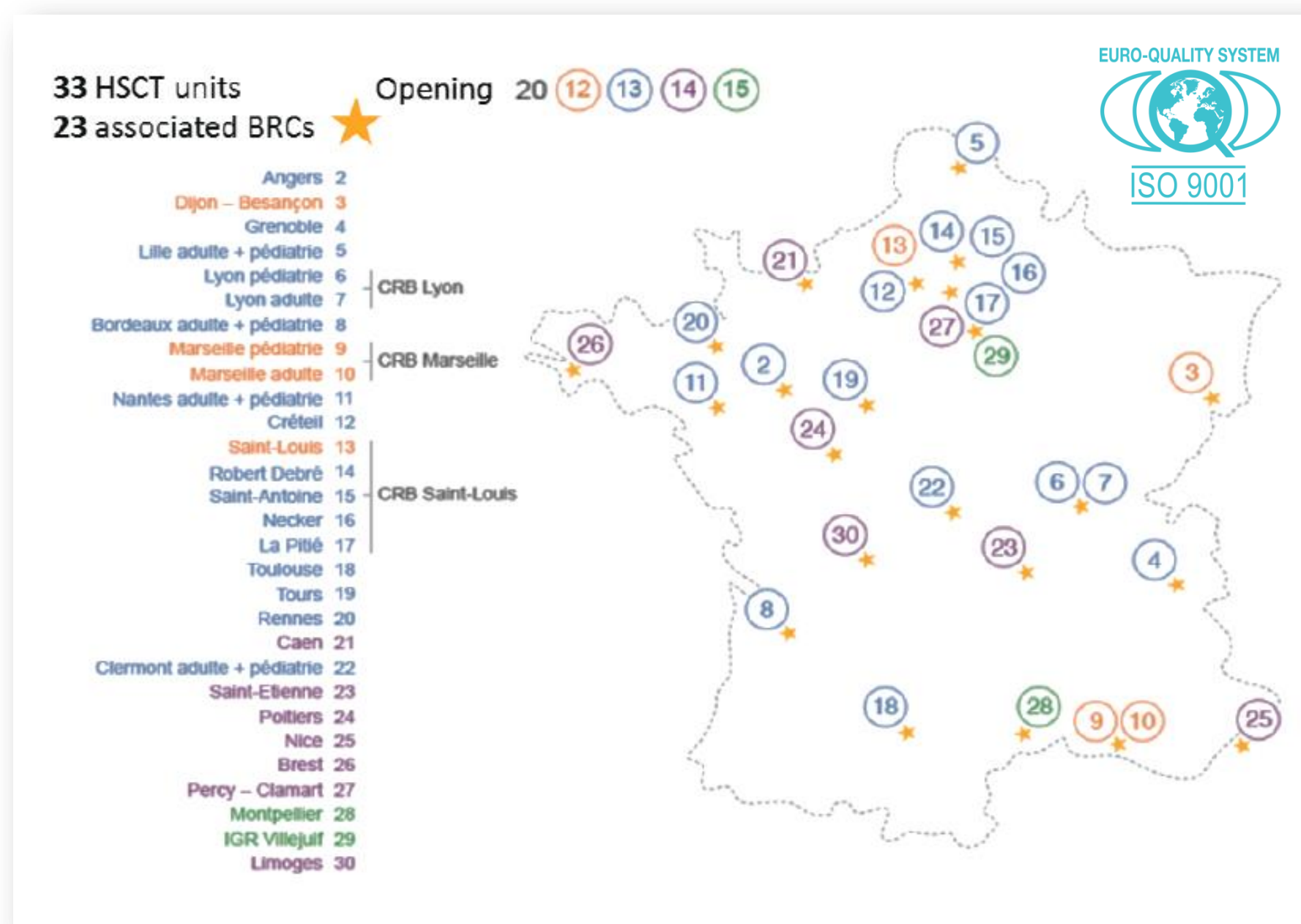
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1 Introduction

Hematopoietic Stem Cell Transplantation (HSCT) is the only curative treatment for numerous blood diseases (such as leukemia, lymphoma, aplastic anemia and others). The main complication is **GvHD**, in which the donor's immune cells recognize the recipient as foreign. The increasing number of unrelated donors, among other factors, means that current levels of GvHD incidence (60%) may rise over the next few years. In patients cured of their hematological diseases, GvHD is the leading cause of death post-HSCT (10 to 20% of patients with GvHD). Lack of knowledge in GvHD physiopathology, along with limited relevant studies (relatively few patients and scarcely any long-term cohorts in the field) explain the absence of curative treatment. In this context, the **CRYOSTEM project** was initiated in 2010 by Prof. Régis Peffault de Latour and Dr. Boris Calmels, and promoted by the Francophone Society for Stem Cell Transplantation and Cell Therapy (SFGM-TC) to establish a **nationwide, prospective and standardized multicenter cohort**. In 2011, CRYOSTEM was founded with the financial support of the French government through the **"National Investment Program"** and granted by patients associations.

2 CRYOSTEM Network Building

CRYOSTEM operates an enlarged and **ISO 9001-certified** network comprising **33 out of the 36 French HSCT Units (adult and pediatric)** and **23 Biological Resources Centers (BRCs)**. In only three years, CRYOSTEM has succeeded in enlisting **more than 400 health professionals** to work together on this collaborative project.



Benefits :

- **High rate of inclusion: 70%** of the French transplanted patients included in CRYOSTEM with a mean rate of inclusion of **100 patients/month**
- **Limited cryo-preservation delays : 60%** of blood samples treated in **less than 4 hours**

4 Research Promotion in the field of GvHD

One of CRYOSTEM initial objectives was supplying the national and international scientific community, from both academia and industry, for **large-scale research on GvHD to increase biomedical knowledge** in the field.

The ultimate goal is to improve the healthcare of transplanted patients by obtaining a **better understanding of GvHD physiopathology** and by **developing predictive tests and treatments**.

Since mid-2015, physicians and scientists have had access to the CRYOSTEM collection via **annual calls for proposals**. **CRYOSTEM Scientific Committee** and **international experts** proceed to the selection and review.

To date, **4 French research projects exploring GvHD** have been granted with almost **3,500 CRYOSTEM samples**. Scientific publications are expected for 2018.

In 2017, CRYOSTEM has received **10 new applications**, including **2 international**. Moreover, **2** of them have already been selected to be granted with the collection samples in the early 2018.

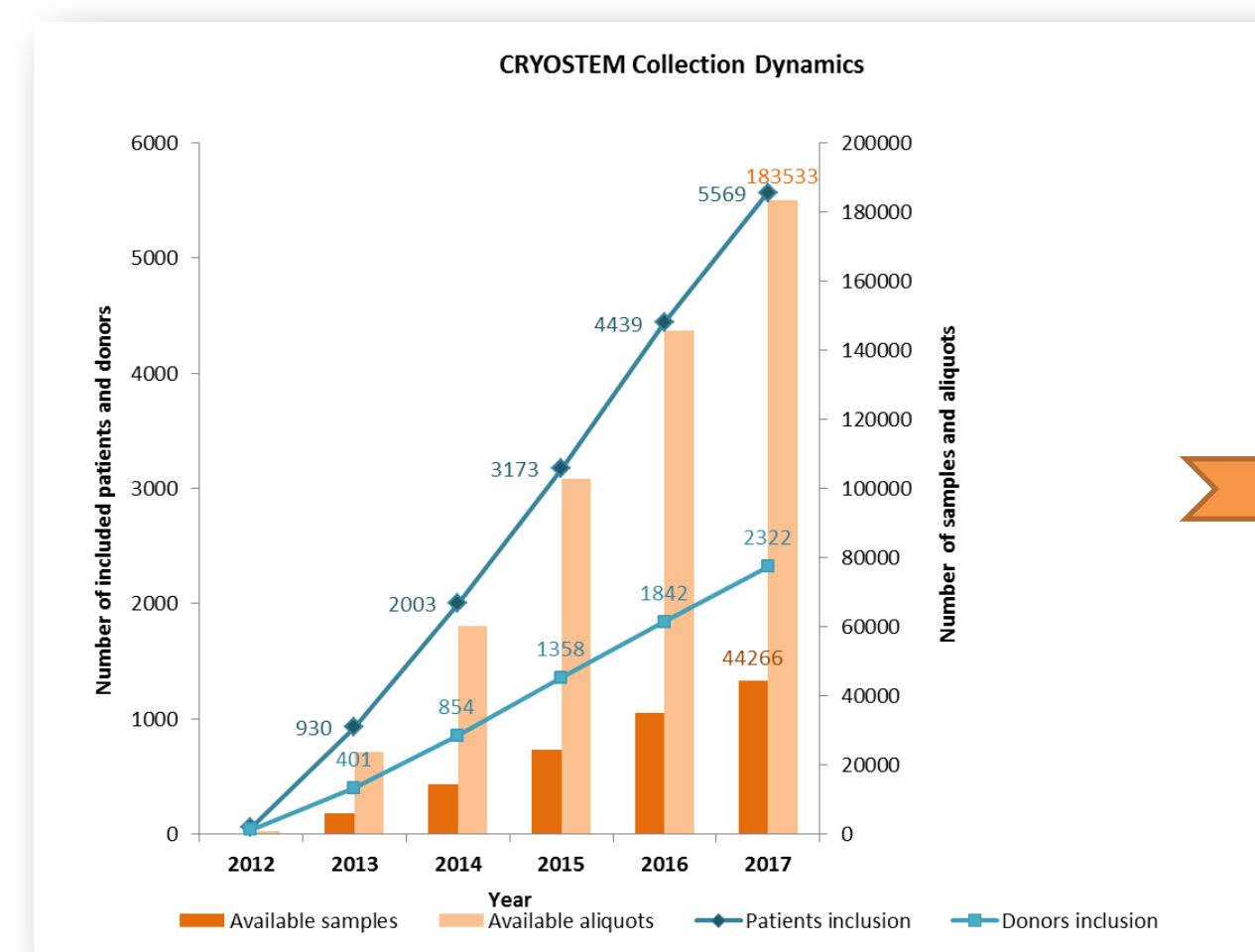
5 Conclusion

CRYOSTEM is the **only biobank in Europe** to connect biological samples with clinical data and HSCT cohorts, firstly dedicated to GvHD. CRYOSTEM has demonstrated its relevance and usefulness to support large-scale researches on GvHD. CRYOSTEM collection is offering a unique opportunity to confirm and expand preliminary results in larger cohorts. Since November 2016, CRYOSTEM thematic enlarged to **all HSCT complications** with the objectives to overcome new fields.

3 CRYOSTEM Collection

In only six years, more than **5,000 patients** and **2,300 donors** have been included in CRYOSTEM (as of December 31, 2017). Blood samples are taken **pre- and post-HSCT** in line with a simple sampling schedule, taking into account **acute and/or chronic appearance of GvHD**.

BRCs process blood samples in line with **standardized and harmonized procedures** so as to establish a high-quality and homogeneous collection, independently at each BRC. **Three sample types** are isolated and cryopreserved from blood samples: **plasma, dried pellets, and viable cells in DMSO**.



Available in CRYOSTEM :

- **37 000 aliquots of acute GvHD**
- **11 000 aliquots of chronic GvHD**
- + **GvHD Clinical data :**
 - Target (skin, digestive, hepatic)
 - Stages
 - Corticosteroid resistance
 - Classification
 - Evolution of the disease

All the well-annotated **clinical data associated to biological samples** are centralized in a unique secure database: the **MBioLims CRYOSTEM**. The MBioLims is also directly linked to the EBMT (European Society for Blood and Marrow Transplantation) European clinical database, **PRoMiSe**.

The first 4 GvHD projects

- #1 – Investigation of a potential association between ILCs and acute and chronic GvHD** (Dr F. Vély and Pr E. Vivier, Marseille, France)
- #2 – Comprehensive assessment of the recovery and potential contribution of MAIT cells in controlling acute GvHD** (Pr S. Caillat-Zucman and Pr JH. Dalle, Paris, France)
- #3 – Validation of plasmatic protein biomarkers of acute and chronic GvHD for predicting and monitoring responses to therapy** (Dr E. Daguindau and Pr PS. Rohrllich, Nice, France)
- #4 – Identification of pathogenic mechanisms involved in acute GvHD by metabolomic and transcriptomic mapping** (Dr D. Michonneau and Pr G. Socié, Paris, France)

2 projects recently selected

- #5 – Predicting complications such as EBV, GvHD and PTLD** (Dr E. Drouet, Grenoble, France)
- #6 – Understanding mechanisms of mortality after acute GvHD to better treat the complication** (Dr T. Luft, Heideberg, Germany)

8 new applications under selection

Already supplied:
 ≈ 2,700 aliquots of cells in DMSO
 ≈ 800 aliquots of plasma



Supplies planned for 2018:
 ≈ 5,000 aliquots (cells in DMSO, plasma and dried pellets)