Findings regarding microparticles in SCD
Inserm 1134 / UA research unit, in Guadeloupe

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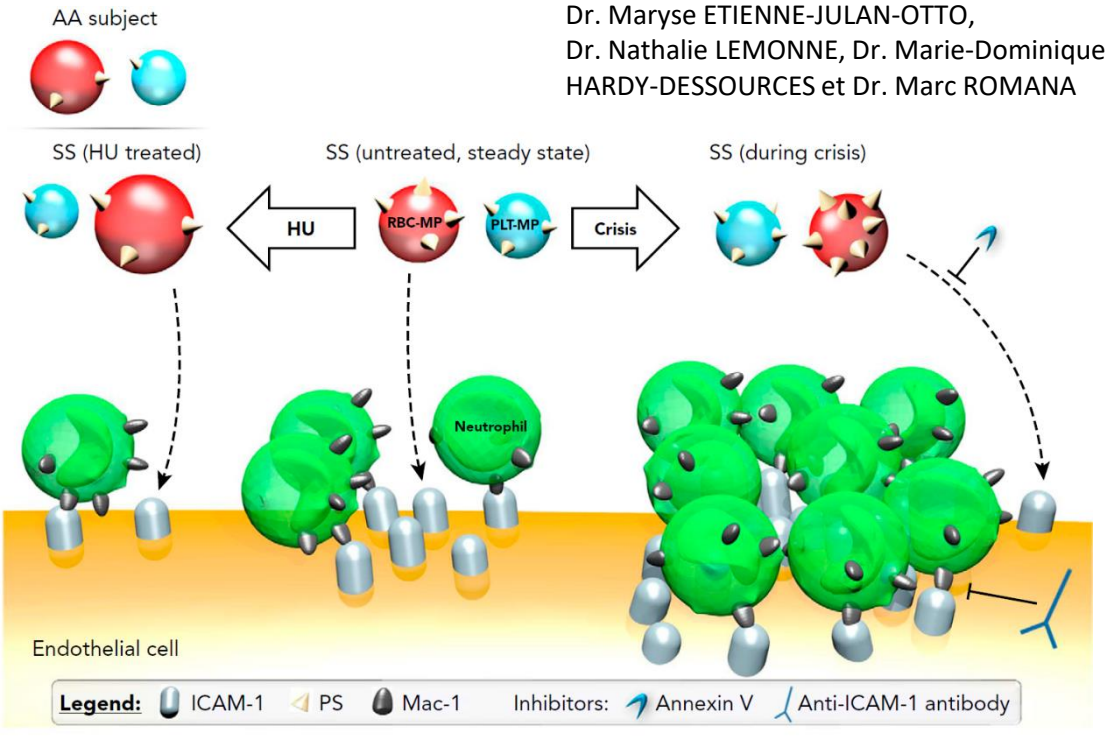
Why studying microparticles?

Microparticles (or **MPs**) are particles released in blood, above all by platelets and red blood cells. They are respectively called PLT-MPs and RBC-MPs. We can easily isolated them, from a blood sample. Whereas they were unknown 40 years ago, MPs are more and more studied since they may help to ameliorate diagnosis precision and even potentially allow to predict or prevent the occuring of a crisis. Therefore we need to better understand their effects on cells lining blood vessels wall (**endothelial cells**).

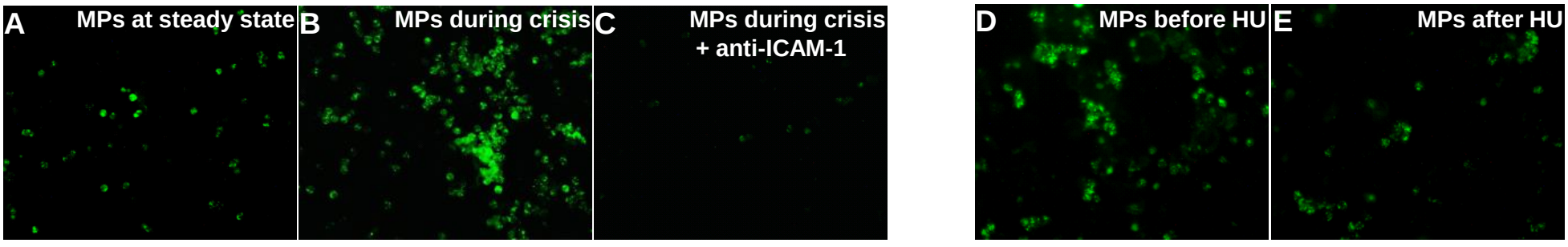
Characteristics and effects of MPs

The image shown against sums up the main recent findings of our laboratory, regarding sickle cell patients' MPs. They are based on several research protocols: HU (article of GARNIER *et al.*, 2017 BJH), Stress (article of HIERSO *et al.,* 2017 BJH) and Sapotille (article of GARNIER *et al.*, Plos One 2017).

During crises, MPs are more numerous at steady state, et exhibit at their surface a higher level of a molecule called PS (or phosphatidylserine). Since a decade, it ha been shown that the majority of vasooclusive crises are due to adhesion of some white blood cells called **neutrophils**, to the wall of small blood vessels. Since neutrophils are large and little deformable, they then trap red blood cells (RBCs), leading to vessel occlusion: the crisis starting point.



As a consequence we cultured endothelial cell, in the presence of MPs, then with neutrophils. In order to visualize adherent neutrophils, they were labelled in green (panels A-E). MPs from patients in crisis, caused more adhesion than MPs from the same patients but at steady state (panels A and B). Moreover, treating patients for 2 years with hydroxyurea (HU, or Sicklos), diminished PS exposure by their MPs and decreased neutrophil adhesion level (panels D and E).



MPs and potential medicines

Other results show that it is thanks to their exposed PS, that MPs can bind to endothelial cells, and so make them more adhesive. Indeed MPs make them expose a sort of hook called ICAM-1 and allowing to retain neutrophils owing to an element at their surface called Mac-1 (see 1st figure).

Therefore we capped the PS of MPs from patients in crisis, using annexine A5. This capping decreased the amount of ICAM-1 that endothelial cells exhibited. We have also used an element that prevents Mac-1 to bind ICAM-1: an anti-ICAM-1 antibody. Consequently, the number of adherent neutrophils drastically decreased (panels B and C).

Conclusions

- MPs facilitate the occuring of crises by increasing the number of adherent neutrophils
- Sicklos (or HU) ameliorates patients' condition by diminishing the quantity of PS exposed by MPs and preventing them from making cells lining blood vessel wall more adhesive
- Annexine A5 and an anti-ICAM-1 antibody could be future medicines to treat sickle cell disease

The importance of all these results has been recognized as they have been published in a journal of the American Society of Hematology, the most prestigious international journal dealing with blood diseases: Blood.

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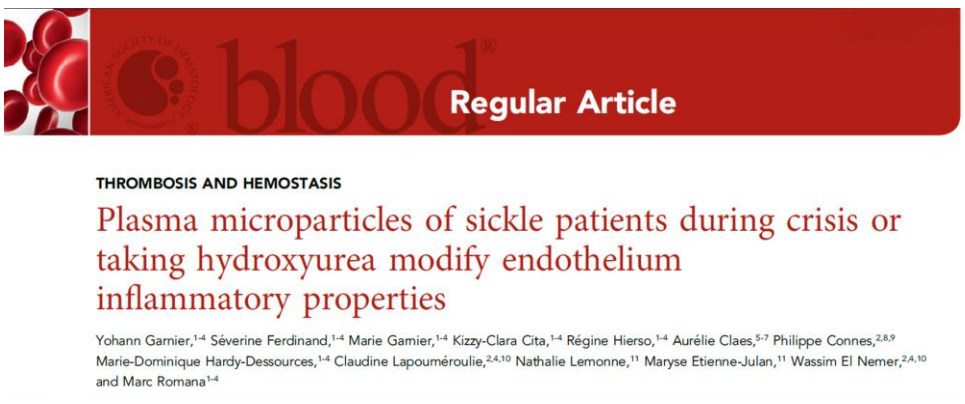
blood Regular Article

THROMBOSIS AND HEMOSTASIS

Plasma microparticles of sickle patients during crisis or taking hydroxyurea modify endothelium inflammatory properties

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