Immunogenetics: Open Access

Mardente et al., Immunogenet Open Access 2018, 3:1

Commentary Open Access

# From Human Megakaryocytes to Platelets: Effects of Aspirin on High-Mobility Group Box 1/Receptor for Advanced Glycation End Products Axis

**Stefania Mardente*, Alessandra Zicari and Marco Tafani**

*Department of Experimental Medicine, University of Rome Sapienza, Viale Regina Elena 324, 00161 Rome, Italy*

***Corresponding author:** Stefania Mardente, Department of Experimental Medicine, University of Rome Sapienza, Viale Regina Elena 324, 00161 Rome, Italy, E-mail: stefania.mardente@uniroma1.it

**Received date:** June 13, 2018; **Accepted date**: June 18, 2018; **Published date:** June 25, 2018



**Citation:** Mardente S, Zicari A, Tafani M (2018) From Human Megakaryocytes to Platelets: Effects of Aspirin on High-Mobility Group Box 1/Receptor for Advanced Glycation End Products Axis. Immunogenet Open Access 2: 120.

**Keywords:** Megakaryocytes; HMGB1

## Commentary

The ongoing molecular investigations on the links between coagulation and inflammation have revealed that HMGB1 acts as a link between the two processes.

HMGB1 is a nuclear protein that has also an active role in the cytoplasm and in the extracellular space. It is released by immune cells and damaged cells as a messenger of "alarm and action".

Moreover, HMGB1 produced by tumor cells is involved in tumor progression and elusion from immune system [1].

Due to its pro-inflammatory and tumoral progression roles, several biologics have been developed in order to inhibit HMGB1, with success in several diseases [2].

As well as monoclonal and polyclonal antibodies that show beneficial effects in shock after trauma or in sepsis, small molecules like glycyrrhizin (Gly), an extract from the licorice plant and aspirin are able to inhibit HMGB1's extracellular activities.

Megakaryocytes (MKs) that mature in the bone marrow, give rise to platelets (PLTs), that are provided with mRNAs and pro-active substances that are involved in hemostasis, thrombosis and inflammation, are the major source of HMGB1. PLTs are able to release HMGB1 as a free molecule and inside exosomes.

Using MKs obtained from human hematopoietic progenitor cell purification [3] from peripheral blood and a human megakarioblastic cell line, we have recently demonstrated that platelets are provided with HMGB1 protein and mRNA by their progenitors and when activated release it with other pro-inflammatory and pro-thrombotic mediators [4].

RAGE (receptor for advanced glycation end products) that binds HMGB1, is also localized in the cytoplasm of MKs and as their maturation progresses it is found in the inner part of the cell membrane and finally on the surface of the buds that give rise to platelets. The RAGE-HMGB1 interaction and consequent release of pro-inflammatory molecules has been shown to play a central role in the pathogenesis of atherothrombosis [5].

Aspirin, one of the most ancient anti-inflammatory drugs, is known to be an inhibitor of COX 1 that is able to modulate platelets' dual function: coagulation and inflammation. We have shown that aspirin has a central role in modulating HMGB1 mRNA and protein expression during the development of megakaryocytes obtained from DAMI cells or by human peripheral blood precursors [6]. Modulation of HMGB1 mRNA and protein expression was also obtained in high thrombotic risk patients and in healthy volunteers who were administered 300/mg aspirin/per os for 2 weeks [6]. Another interesting observation of this study is that aspirin also reduces the expression of RAGE in DAMI cells, MKs and their derived PLTs. The interaction of aspirin with RAGE is not direct but is probably due to its interaction with HMGB1 that modulates RAGE expression with a positive feedback mechanism.

Taken together, our results suggest that the decreased expression of both HMGB1 and RAGE, by modulating both coagulation and inflammation could be of great significance in the reduction of cardiovascular complications.

## References

1. Fuentes E, Palomo I, Rojas A (2016) Cross-talk between platelet and tumor microenvironment: Role of multiligand/RAGE axis in platelet activation. Blood Rev 30: 213-221.
2. Venerau E, De Leo F, Mezzapelle R, Careccia G, Musco G, et al. (2016) HMGB1 as biomarker and drug target. Pharmacol Res 111: 534-544.
3. Guerriero R, Testa U, Gabbianelli M, Mattia G, Montesoro E, et al. (1995) Unilineage megakaryocytic proliferation and differentiation of purified hematopoietic progenitors in serum-free liquid culture. Blood 86: 3725-3736.
4. Langer HF, Weber C, Gawaz M (2013) The platelet—thrombosis and beyond. Thromb Haemost 110: 857–858.
5. Fuentes E, Rojas A, Palomo I (2016) NF-κB signaling pathways as target for antiplatelet activity. Blood Rev 30: 309-315.
6. Mardente S, Mari E, Massimi I, Tafani M, Guerriero R, et al. (2018) From Human Megakaryocytes to Platelets: Effects of Aspirin on High-Mobility Group Box 1/Receptor for Advanced Glycation End Products Axis. Front Immunol 8: 1946.