

## **Monocyte Subsets in Rat following Myocardial Infarction**

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Background and aims: Monocytes and macrophages are key players in the healing process that ensues following myocardial infarction (MI). Myocardial infiltration by monocytes facilitates the scavenging of apoptotic neutrophils and necrotic cardiomyocytes, and modulates cardiac remodeling. Monocytes subset differentiation post-MI is characterized in mice and humans whereas only limited such information is available in rats. The aim of this study was to characterize markers that will enable in vivo study of rat monocytes subsets behavior following MI.

Methods and results: Monocytes level was measured by flow cytometry using anti-CD68 (ED1) antibody. Cells size and granularity confirmed CD68 as a good marker for monocytes count. Anti-CD43 antibody enabled differentiation of two monocytic subsets: pro-inflammatory (ED1+ CD43<sup>lo</sup>) and anti-inflammatory (ED1+ CD43<sup>hi</sup>). Blood was drawn before (baseline), and at 5 days and 8 days after permanent ligation of the left descending coronary artery. At baseline, the pro: anti inflammatory monocytes ratio was 30:70, respectively. Following MI the relative monocytes count (% from WBC) was augmented from  $8.6 \pm 2.7$  at baseline to  $10.2 \pm 1.6$  at day 5 and  $13.3 \pm 1.82$  at day 8 (n=6). The increase in relative monocytes count at day 5 was due to an increase in the ED1+CD43<sup>lo</sup> monocytes (pro-inflammatory) from  $2.3 \pm 0.5$  at baseline to  $4.15 \pm 0.7$  at day 5 (n=6, p<0.001). Three days later, the increase in monocytes count was due to an increase in ED1+CD43<sup>hi</sup> monocytes (anti-inflammatory) from  $5.7 \pm 1.6$  at day 5 to  $9.2 \pm 1.8$  at day 8 after MI (n=6, p<0.02).

Conclusions: Two subsets of monocytes were characterized in rats at baseline and following MI. In accordance to the literature we showed that the initial increase (day 5) is due to pro-inflammatory monocytes, whereas later (day 8) the anti-inflammatory monocytes population is increased. Monocyte subsets study will allow us to study the intricate inflammatory response to myocardial infarction and healing.