Effects of low dose radiation on atherosclerosis in APOE(-/-) mice: study of short term effects on macrophage polarization

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EFFECTS OF LOW DOSE Γ RADIATION ON ATHEROSCLEROSIS IN APOE(-/-) MICE: STUDY OF SHORT TERM EFFECTS ON MACROPHAGE POLARIZATION .

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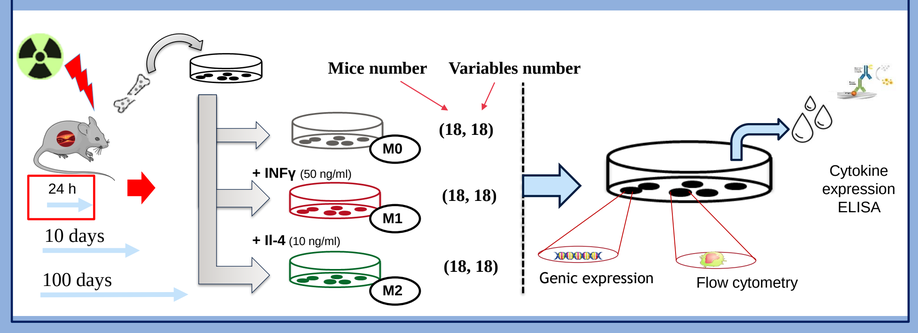
I. Study objective

Athersoclerosis is a chronic inflammatory disease of medium and large arteries that can lead to myocardial infarction or stroke. Mechanistic understanding of the effects of low-dose ionizing radiation (LDIR) on atherosclerosis remains incomplete. The experimental studies have shown a protective effect of LDIR on atherosclerosis in rodent models. However early responses of LDIR in different cell types that are known to be involved in atherosclerosis is not clear. The objective is to understand biological mechanisms of LDIR include on experimental animal groups with multimodal approach. In this study, we report results of applying the fold-change, usually considered a relevant criterion for stating difference and similarity between measurements and a multilevel multivariate approach. Revealing complex correlations and causal links related to health conditions, such as atherosclerosis, can help advance the concept adverse outcome pathway (AOP).

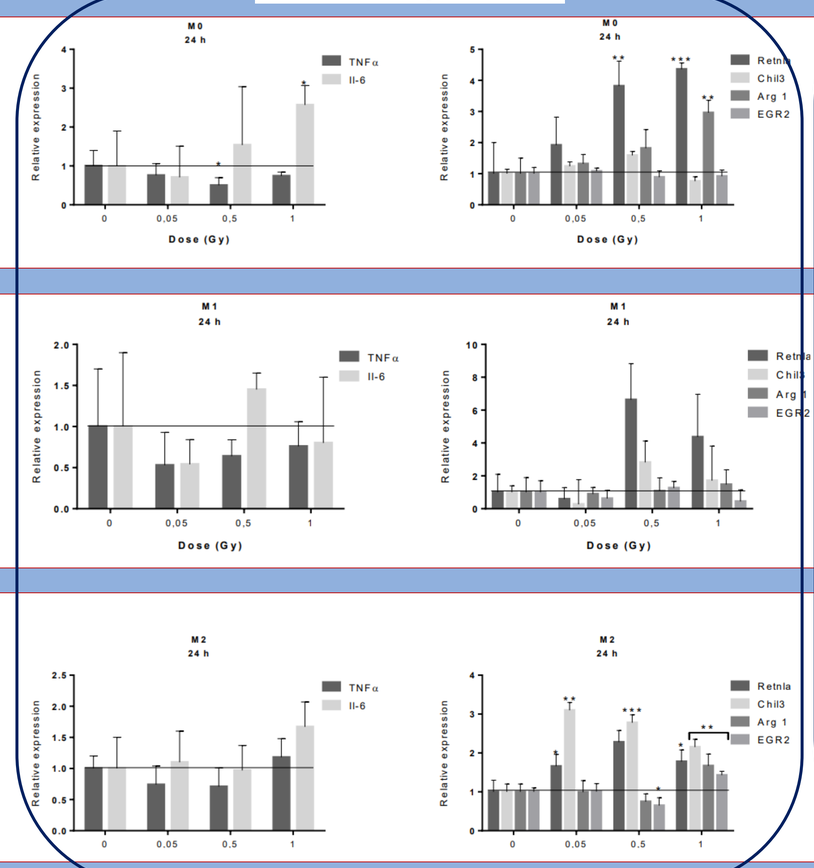
Study Design



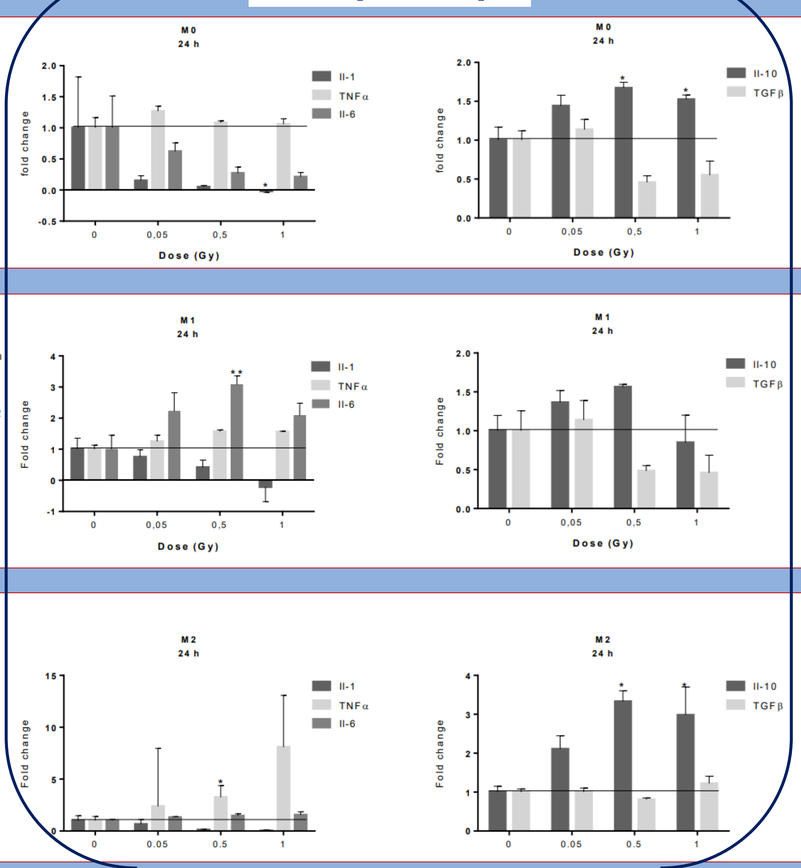
Study Results

24h ← **1) Fold change vs control mice** → 24h, 10Days, 100Days

Genetic Expression



Flow cytometry



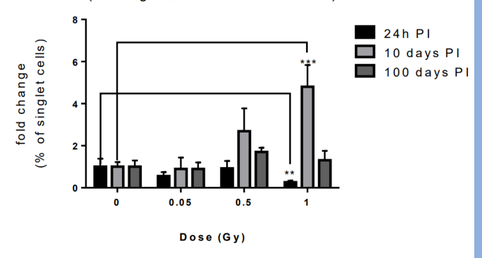
M0

M1

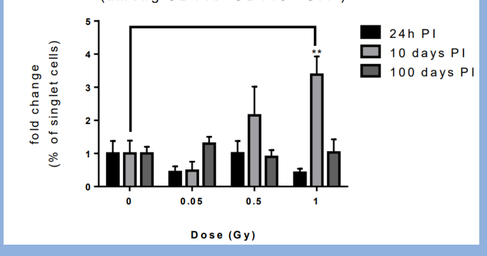
M2

Circulating blood

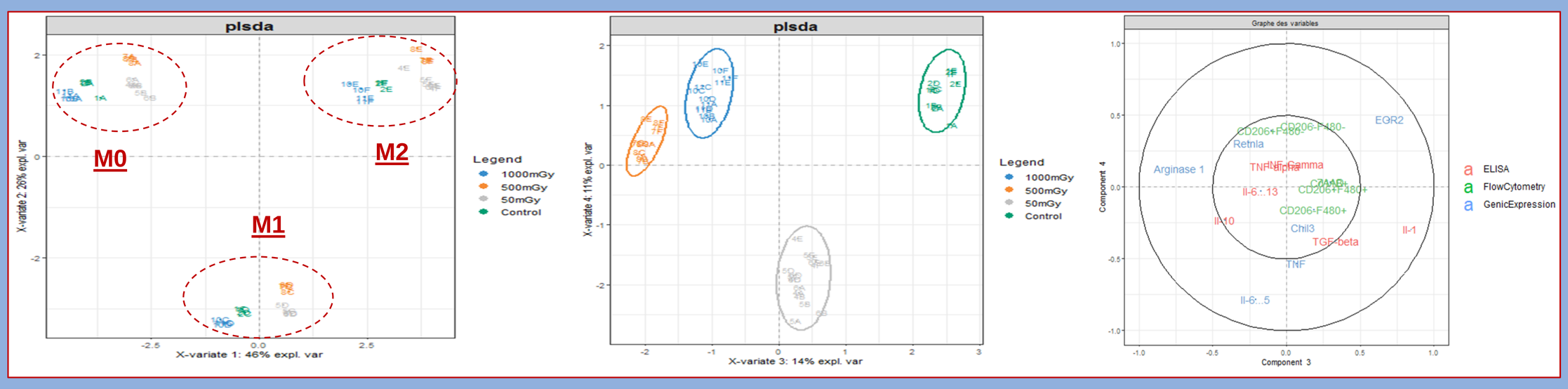
Ly6C^{high} monocytes (among CD11b+CD115+ Gr1-)



Ly6C^{Low} monocytes (among CD11b+CD115+ Gr1-)



2) Multilevel multivariate approach (24h)



Conclusion

We found a significant dose-dependent increase of genic expression of Chil-3 and Retnla anti-inflammatory markers in M0 and M2 type macrophages upon 24 hours exposure and no effects on M1types. These effects were associated with a dose-dependent increase of IL-10 and reduction of IL-1 secretions in M0 and M2 and an increase of IL-6 in M1 type macrophages. Circulating pro-inflammatory Ly6CHigh monocytes were reduced at 24 hours and anti-inflammatory Ly6Clow monocytes were notably increased in the spleen 100 days upon irradiation.