

# EFFECTS OF LOW DOSE $\Gamma$ RADIATION ON ATHEROSCLEROSIS IN APOE(-/-) MICE: STUDY OF SHORT TERM EFFECTS ON MACROPHAGE POLARIZATION

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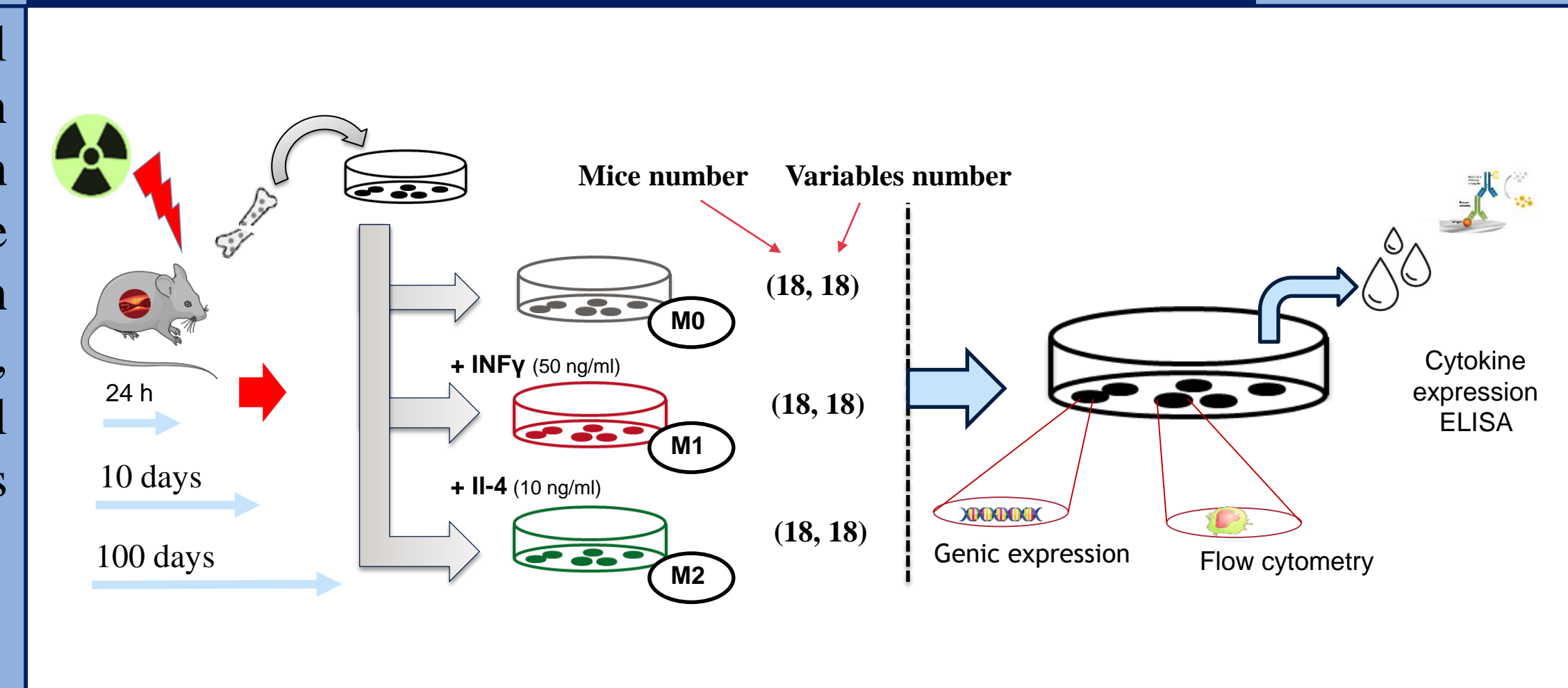
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## I. Study Objective

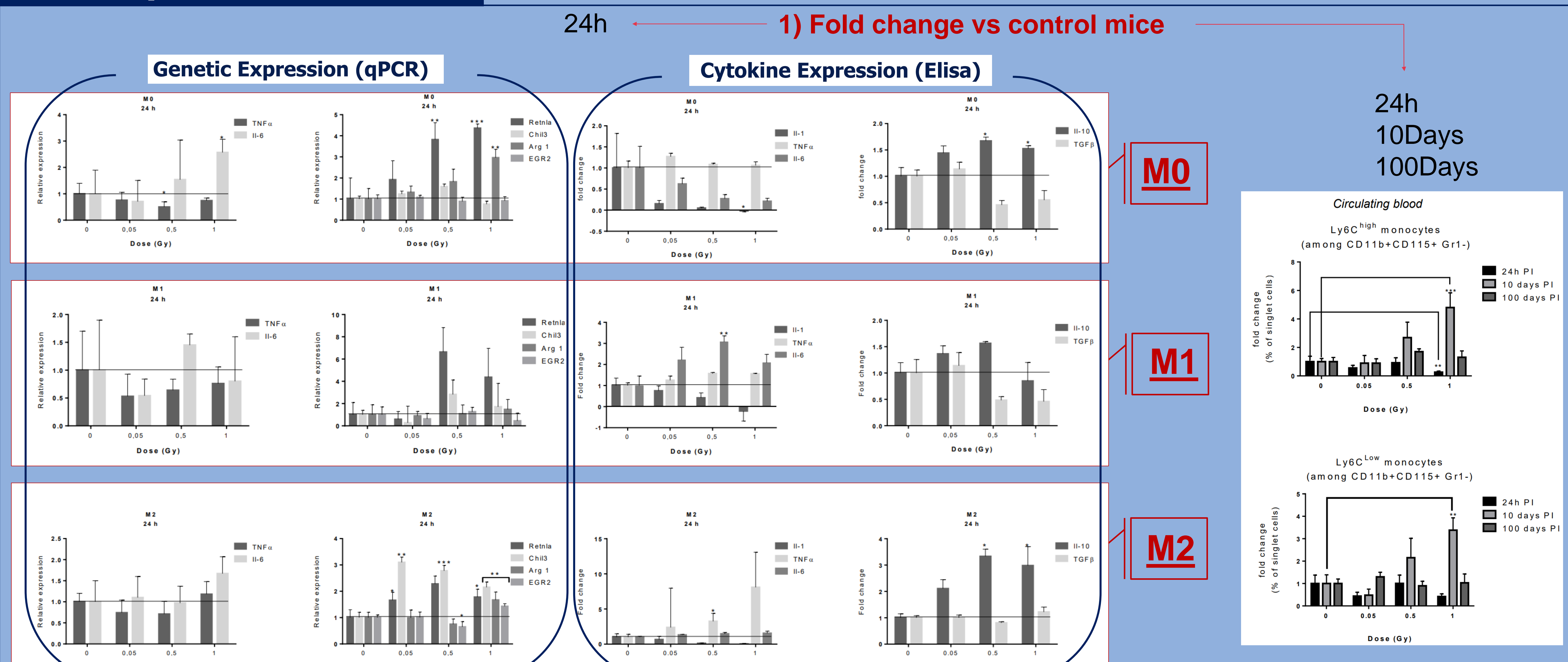
Atherosclerosis is a chronic inflammatory disease of medium and large arteries that can lead to myocardial infarction or stroke. Mechanistic understanding of the effects of low-dose ionizing radiation (LDIR) on atherosclerosis remains incomplete. The experimental studies have shown a protective effect 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 different approaches. 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[1]. Revealing complex correlations and causal links related to health conditions, such as atherosclerosis, can help advance the concept adverse outcome pathway (AOP).

[1] Liqueur, B. Lê Cao, K-A., et al. (2012). A novel approach for biomarker selection and the integration of repeated measures experiments from two platforms, BMC Bioinformatics, 13:325.

## II. Study Design

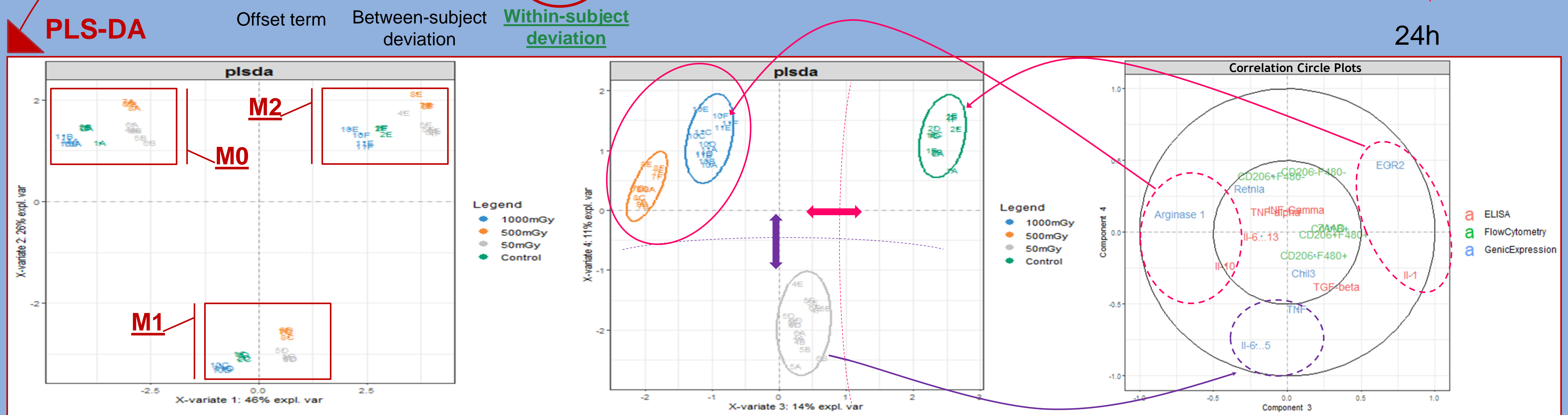


## III. Study Results



$$X = X_m + X_b + X_w$$

### 2) Multilevel multivariate approach [1]



## IV. Study 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 M1 types. 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 blood 100 days upon irradiation. The multilevel approach aims at highlighting the macrophages effects within mice separately from the biological variation between biological samples, which allows to have new biological hypotheses. These results indicate an atheroprotective effect of low to moderate doses of ionizing radiation in an atheroprone mouse model through regulation of macrophages.