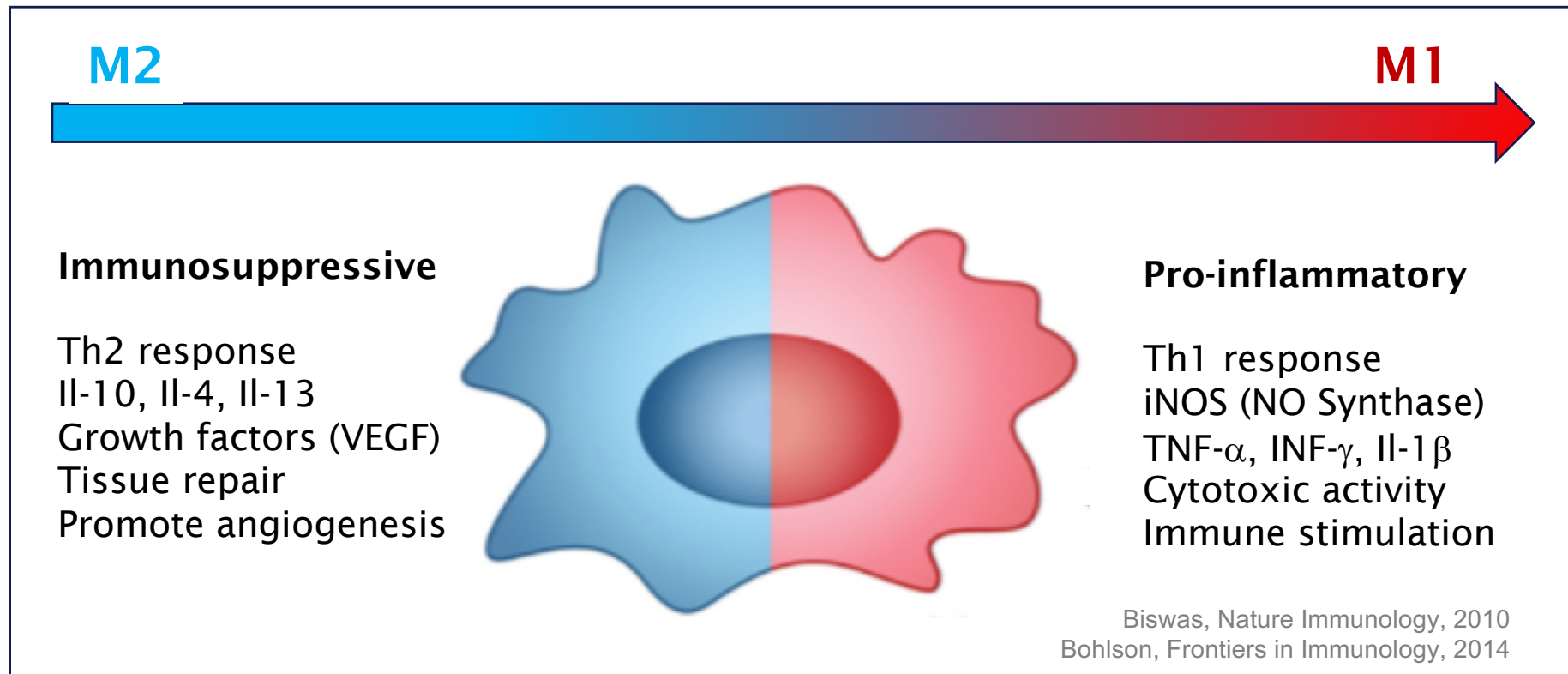


Short-course radiotherapy promotes anti-tumor macrophages via exosomes in human rectal cancer

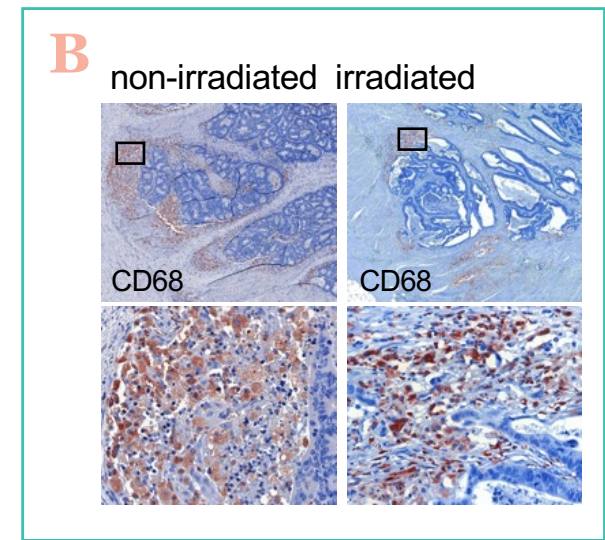
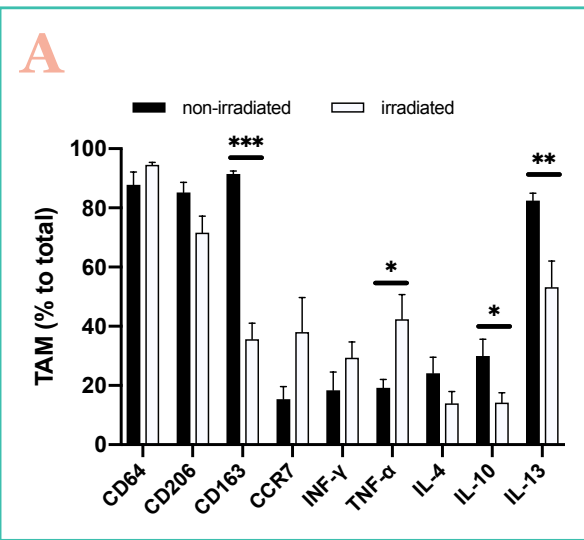
Stary V, Wolf B, List J, Unterleuthner D, Talic M, Längle J, Beer A, Strobl J, Stary G, Dolznig H, Bergmann M
Department of Surgery, Medical University of Vienna, Austria



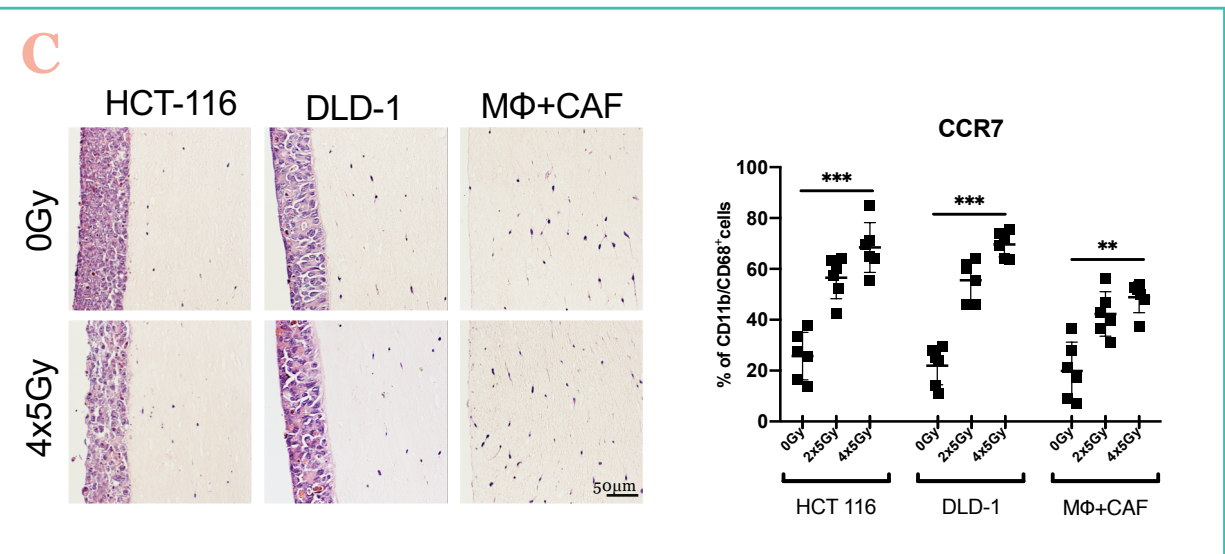
Ex vivo γ -irradiation induces polarization of TAM

Phenotype of tumor associated macrophages (TAM) after *ex vivo* irradiation in human colorectal cancer with flow cytometry (A)

Distribution of TAM in rectal cancer patients after short course radiotherapy with immunofluorescence staining (B)



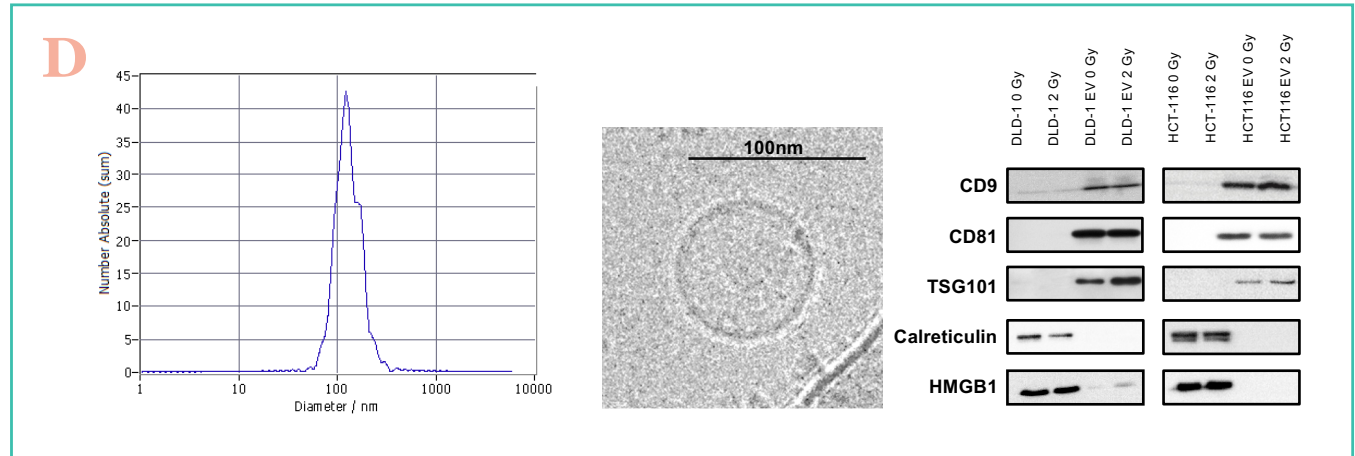
Irradiated organotypic cultures consisting of cancer associated fibroblasts, monocyte-derived macrophages and cancer cell lines (C)



Irradiated DLD-1 exosomes mediate polarization of macrophages

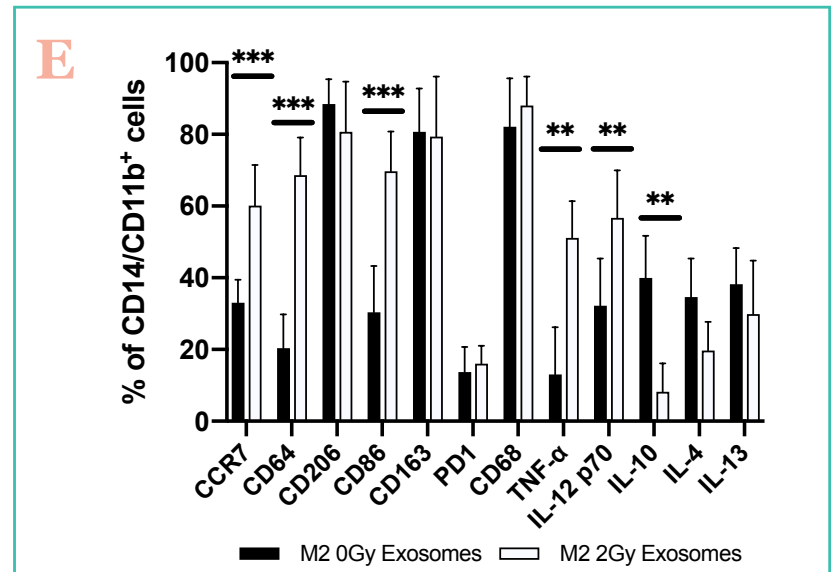
Exosomes isolated from cancer cell lines with ultracentrifugation.

Analysed with nanotracker, electromicroscopy and characteristic markers with western blot (D)



Co-culture experiments with PBMC-derived macrophages and exosomes harvested from cancer cell lines.

Polarization of macrophages can be facilitated by irradiated DLD-1 derived exosomes (E)



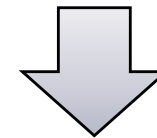
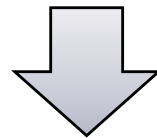
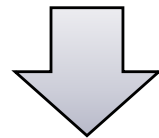
Results

- Tissue sections of patients after low dose hyperfractionated radiotherapy demonstrated a decrease of leukocyte populations
- FACS analysis of human rectal cancer revealed a shift towards M1-like (proinflammatory) markers in macrophages due to irradiation
- Exosomes isolated from irradiated colorectal cancer cell lines induced polarization towards the proinflammatory M1-like phenotype compared to exosomes of non-irradiated cells in co-culture experiments
- Exosomes isolated from irradiated cancer cell lines were enriched for HMGB1 compared to non-irradiated



Conclusion

- Macrophages are effector cells upon irradiation by enhancing their anti-tumoral activities
- Tumor derived exosomes support polarization of macrophages upon irradiation
- Potential cell-to-cell crosstalk through HMGB1



Macrophage-centered approaches to anticancer therapy?

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