Adenosine-Blended Electrospun Scaffolds for Antioxidant and Immune Modulation in Radiation-Induced Hypothyroidism

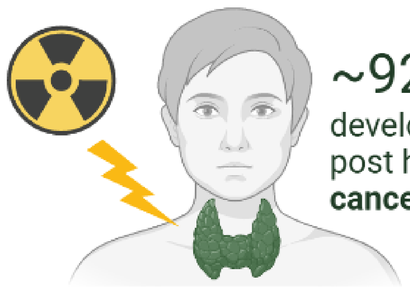
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Radiation-Induced Hypothyroidism (RIHT)



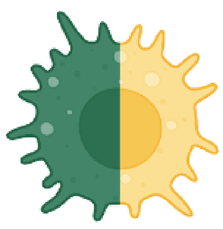
~92% of patients develop **thyroid damage** post head and neck **cancer irradiation (IR)** [2]



Thyroid hormone (T4) replacement is **not curative** and often does not relieve **widespread symptoms** [3]



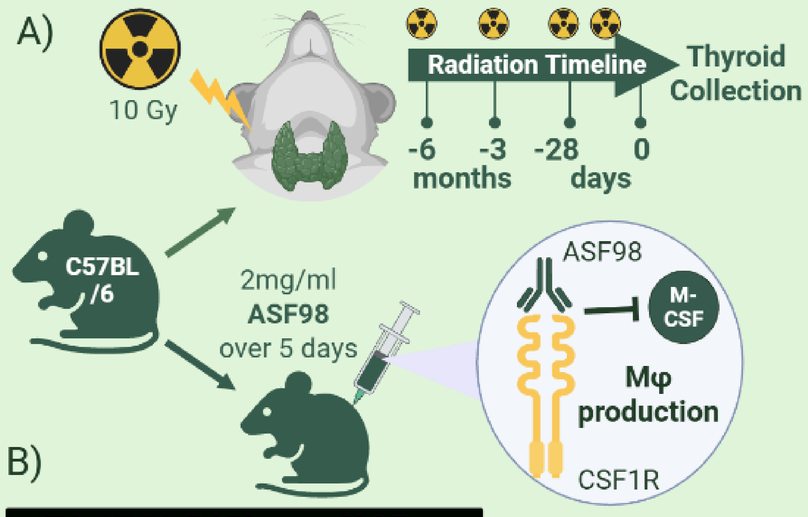
Reactive oxygen species (ROS) and **fibrosis** have been indicated as contributor to **RIHT progression** [4]



Adenosine can shift **macrophage (Mφ)** immune subsets towards a **tissue reparative** phenotype [5]

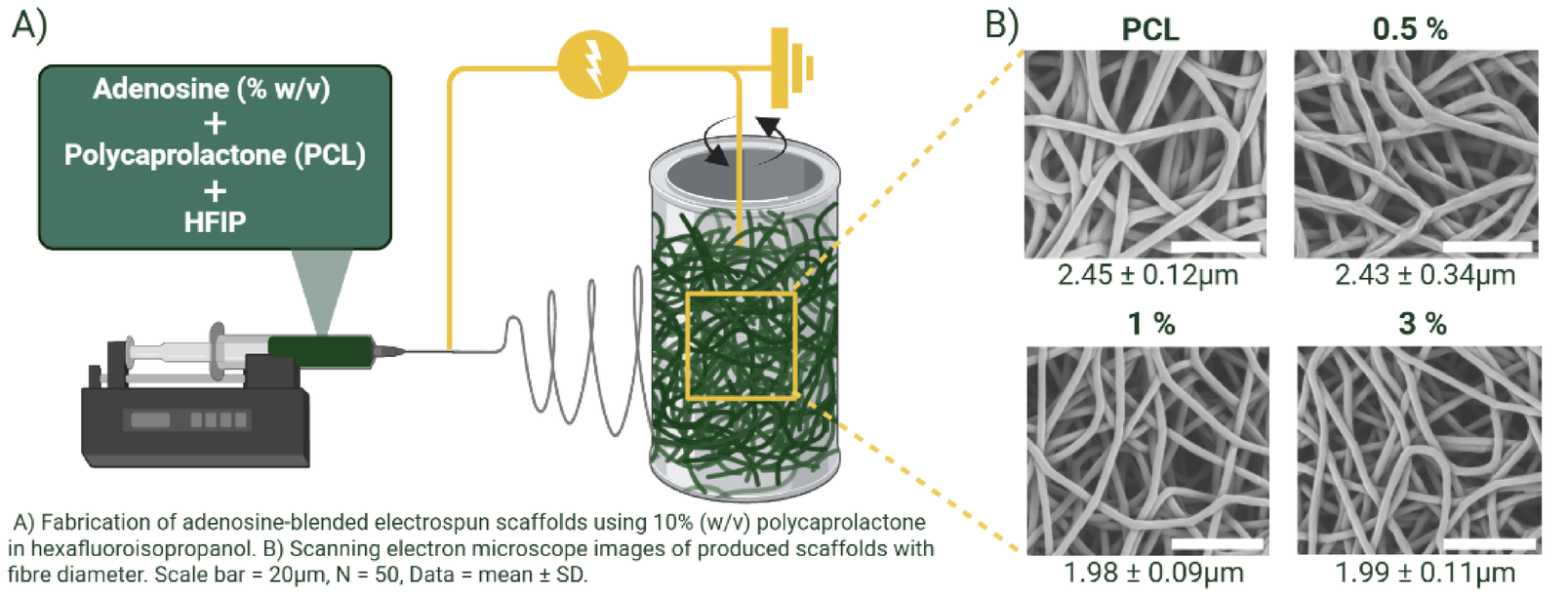
Methodology & Results

RIHT *In Vivo* Model

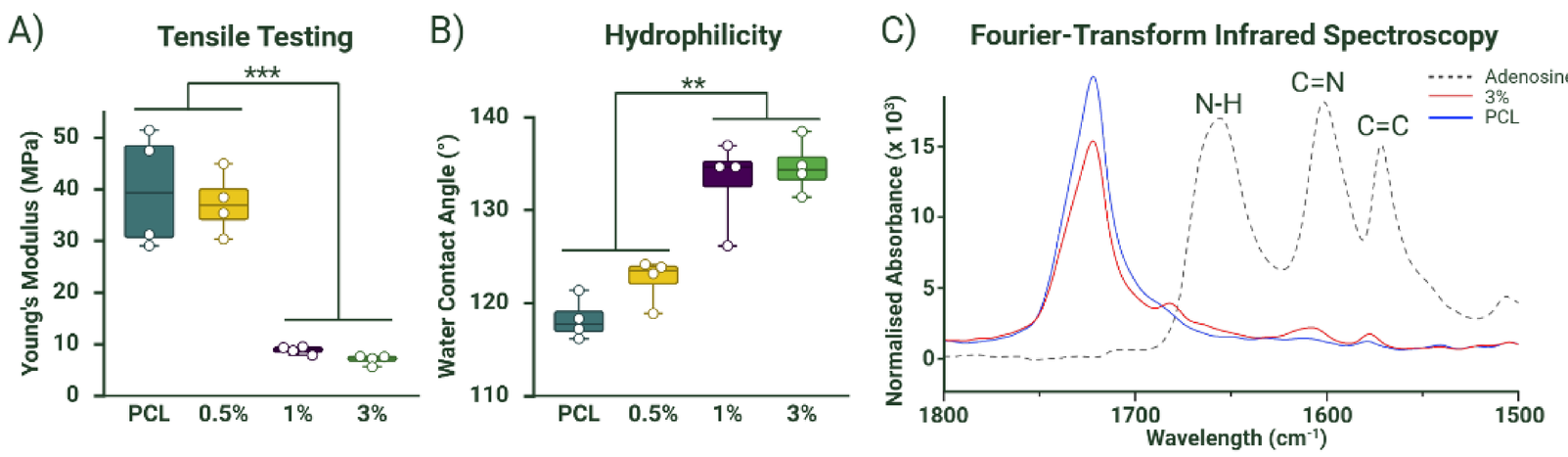


A) Radiation timeline of murine RIHT model (top) and anti-CSF1R treatment for (bottom) . B) T4 (cyan), keratin 8 (KRT8, magenta), and DAPI (yellow) staining of murine thyroid sections (left), and H&E staining (right) Scale bar = 40μm. C) T4 relative mean fluorescent intensity (RMFI). Data = mean ± SD. N = 6. One-way ANOVA with Tukey post-hoc . *p < 0.05, ***p < 0.005

Adenosine Scaffold Fabrication & Characterization

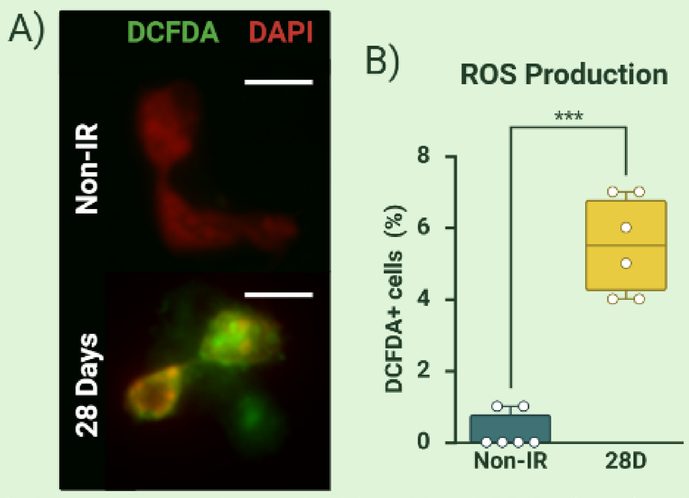


A) Fabrication of adenosine-blended electrospun scaffolds using 10% (w/v) polycaprolactone in hexafluoroisopropanol. B) Scanning electron microscope images of produced scaffolds with fibre diameter. Scale bar = 20μm, N = 50, Data = mean ± SD.



Scaffold material characterization showing A) Young's Modulus B) water contact angle measurement, N = 4, Data = mean ± SD, One-way ANOVA with Tukey post hoc **p<0.01, ***p<0.005, and C) Fourier-transform infrared spectroscopy, indicating spectral shifts due to N-H bending and mixed C=N and C=C stretching

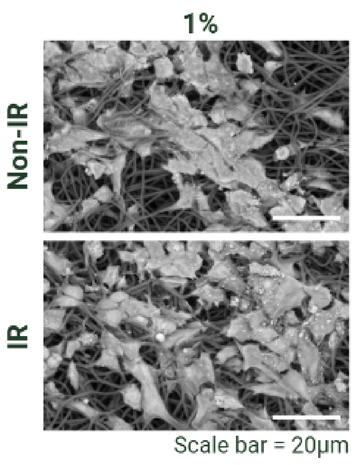
Radiation-Induced Oxidative Stress & Antioxidant Scaffold Effects



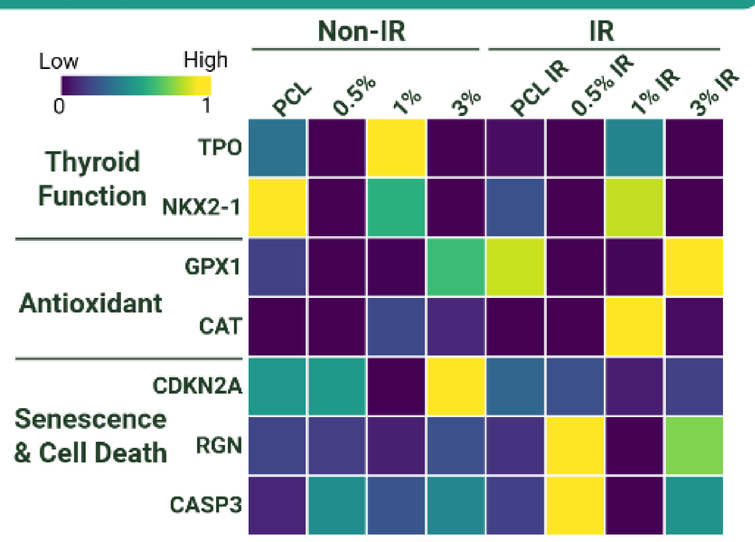
A) Murine thyroid sections stained for ROS with DCFDA (green) and DAPI (red) Scale bar = 10μm. B)% of DCFDA + cells pre- and 28 days post-IR. Data = mean ± SD. N = 6. Independent student's t-test ***p < 0.005

Scaffold Assessment with Irradiated Nthy-ori 3-1 Thyrocytes over 14 days

- **1%** adenosine scaffolds **promoted thyroid-specific gene** expression, regardless of IR
- **1%** and **3%** adenosine scaffolds **upregulated antioxidant** gene expression



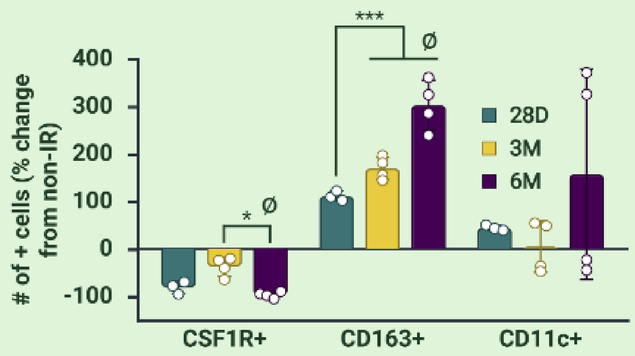
Scale bar = 20μm



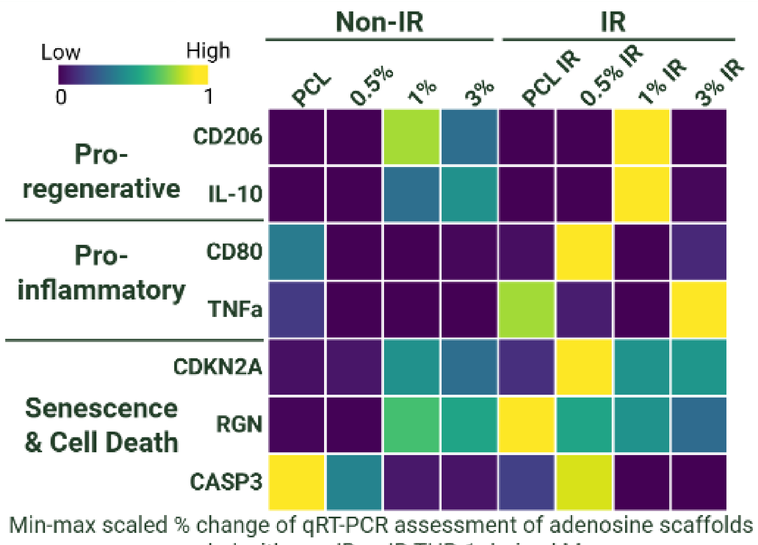
Min-max scaled % change of qRT-PCR assessment of adenosine scaffolds seeded with non-IR or IR Nthy-ori 3-1 cells

Radiation-Induced Mφ Modulation & Reparative Scaffold Effects

Post-IR Mφ Compartment



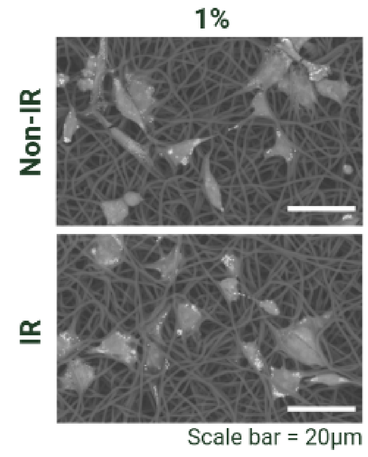
# of cells identified + for CSF1R, CD163 or CD11c via flow cytometry . % change has been calculated from the non-IR control. Data = mean ± SD. N = 4. Two-way ANOVA with Bonferroni post-hoc *p < 0.05, ***p < 0.005, ø = statistical significance compared to non-IR



Min-max scaled % change of qRT-PCR assessment of adenosine scaffolds seeded with non-IR or IR THP-1-derived Mφ

Scaffold Assessment with Irradiated THP-1-derived Mφ over 14 days

- **1%** adenosine scaffolds **promoted pro-regenerative Mφ** marker expression, regardless of IR
- All **adenosine**-containing scaffolds **downregulated senescence**-associated gene expression



Scale bar = 20μm

Conclusion

Adenosine scaffolds increase **antioxidant** gene expression in **thyrocytes**

Adenosine scaffolds shift **Mφ** to a **reparative** phenotype

Following in vivo testing, **adenosine scaffolds** may present a **curative implant** for **RIHT**

Acknowledgements & References

1. *Heim et al., Adv. Healthc. Mat. 3:e01857, 2026*
2. *Zhou et al., J Cancer, 12(2): 451, 2021*
3. *Heim et al., Front Endo, 13, 2022*
4. *Wongwattananard et al., J Radiat Res. 19;65(1) 2024*
5. *Devi et al., Immunobio, 228(3) 2023*

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