THE IRRADIATION-INDUCED RENAL ISCHEMIC PRECONDITIONING IS BLUNTED BY THE ORAL ADMINISTRATION OF THE ANTI-ANGIOGENIC AGENT, SUNITINIB

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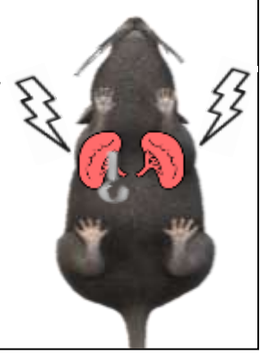
Introduction

Irradiation has been suggested to induce renal ischemic preconditioning (RIP) in mice, possibly via angiogenesis. First, we comprehensively investigate the pathways involved in kidney-centered irradiation. Next, we assess the functional impact of renal irradiation (IRR) applied before renal ischemia/reperfusion (I/R) injury. Finally, we test whether Sunitinib-mediated inhibition of angiogenesis prevents irradiation-associated RIP.

Methods

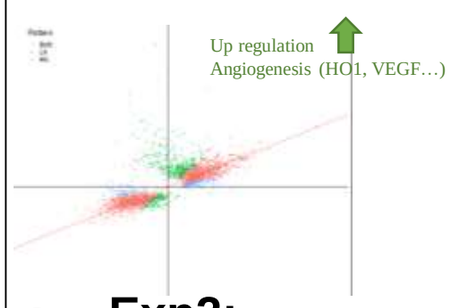
- Exp1: Renal IRR (8.56 Gy) was performed in male C57bl/6 mice (n=10). One month later, total kidney RNA was extracted from irradiated and control (n=5) mice for comparative RNA-Seq.
- Exp2: After renal IRR, the right kidneys were removed, and the left kidneys underwent renal ischemia (30min) / reperfusion (48h) at Days 7-14-28 post-IRR (n=8).
- Exp3: Following the same protocol of I/R at Day14, 3 groups were compared (n=8): 1/ IRR; 2/ IRR and gavage with Sunitinib from Day2 to 13; 3/ control group without irradiation or Sunitinib



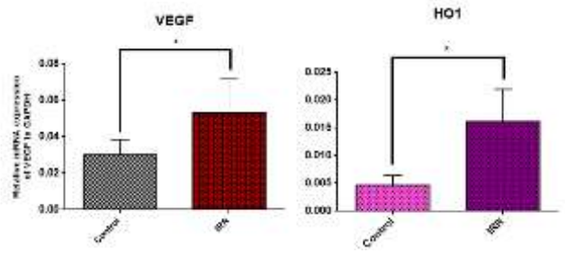
Results

Exp1:

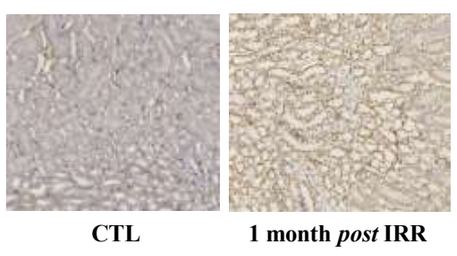
RNA-Seq:

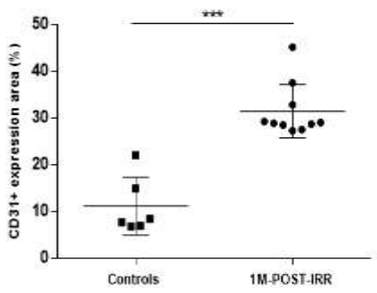


RT-qPCR:



CD31 Immunostaining:





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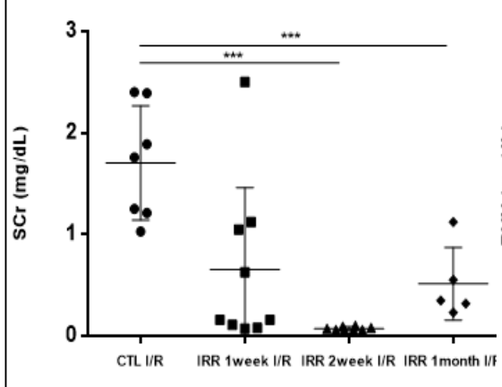
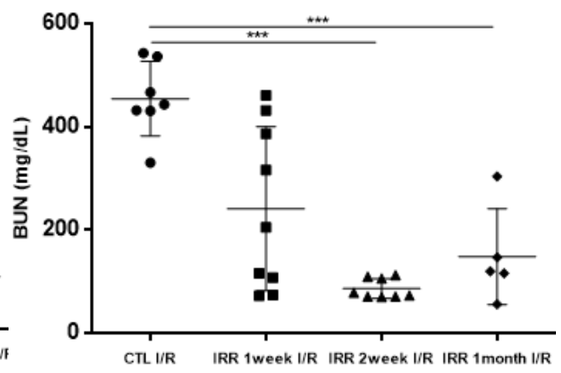
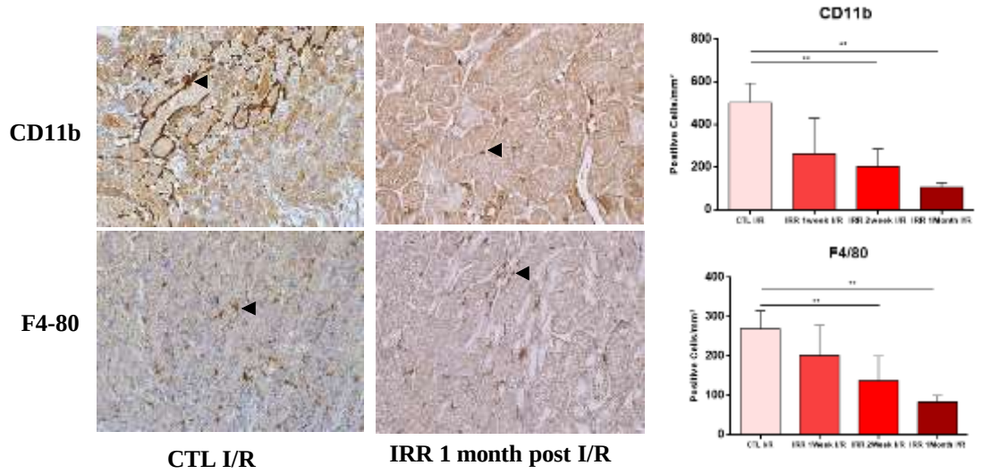
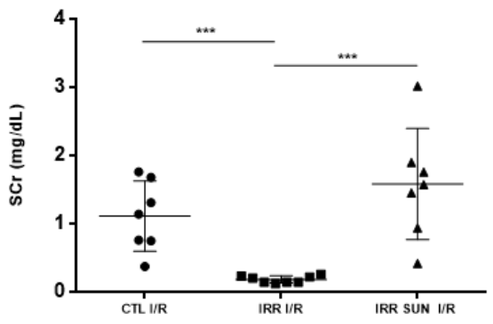
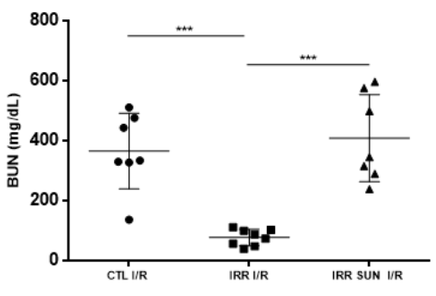


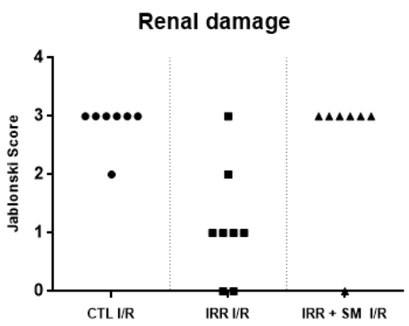




Exp3:







Conclusion

- Kidney-centered irradiation induces the activation of angiogenesis-related pathways in mice
- Renal irradiation leads to RIP, with preserved renal function and attenuated inflammation post I/R
- Exposure to the anti-angiogenic drug Sunitinib post-irradiation prevents the irradiation-induced RIP.

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