Angiotensin II as a linking factor in cardiovascular disease enhanced cancer growth

Benji van Berlo, Celine Civati, Pierangela Esposito, Gilles W. de Keulenaer, Pieter-Jan Guns, Vincent F.M. Segers
Antwerp University, department PhysioFarmacology

INTRODUCTION

Several publications have demonstrated that cardiovascular diseases (CVD) promote tumor growth in mouse models of breast, lung, and colon cancer, suggesting a causal relationship between both diseases.

Recent reports also suggest a link between hypertension and lung cancer, and between cardiac hypertrophy and breast cancer. Angiotensin II (ANGII) is a hormone involved in blood pressure regulation, vascular hemostasis and hypertrophy development. Moreover, ANGII is cancerogenic by increasing proliferation of several cancer cell types. Here we investigated whether ANGII induced CVD could enhance cancer growth.

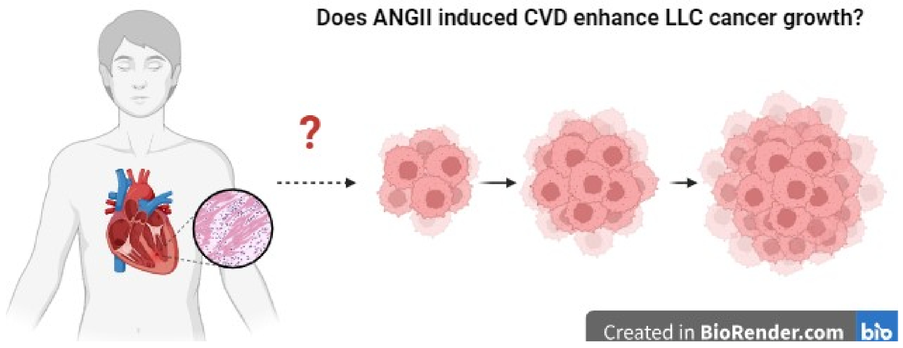
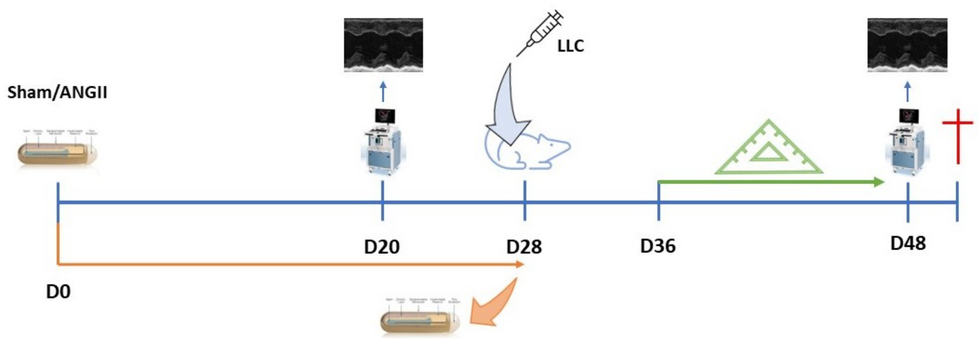


Figure 1. Display of project hypothesis

METHODS

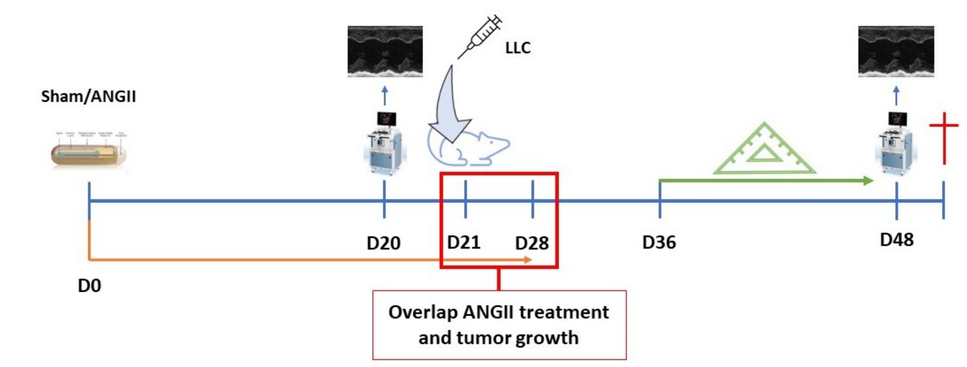
I) Effect of ANGII induced CVD on LLC tumor growth

ANGII (2000ng.kg-1.min-1; 4w) was administered to 10w old C57B6/J mice using subcutaneous osmotic minipumps. At 4w, $5*10^5$ Lewis lung carcinoma (LLC) cells were injected into the right flank. Tumor growth was monitored over 21d using a digital caliper. On day 22, mice were sacrificed for further post-mortem analysis. Figure 2 directly below shows the experimental set-up.



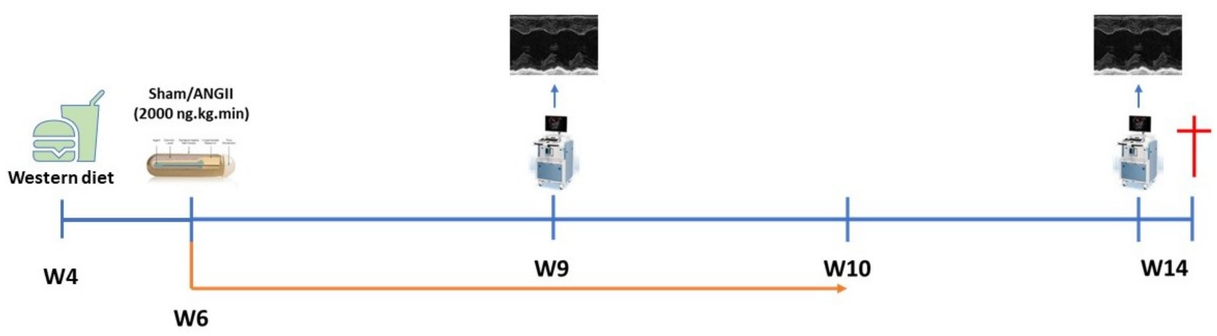
II) Direct impact of ANGII on LLC tumor growth by concomitant treatment and tumor growth

LLC tumor cells were injected at day 21 to have a 7 day overlap with the ANGII treatment. Pumps, cells were placed and injected as mentioned above. Figure 3 directly below shows the experimental overview



III) Impact of ANGII on APC- small and big intestinal tumor growth

APC- mice were fed a high fat diet from the age of 4w. At 6w osmotic mini pumps releasing 2000 ng.kg.min of ANGII were placed subcutaneously on the right flank . At 14w mice were sacrificed and the number of polyps, tumors in the small intestine (SI) and colon counted. Figure 4 below shows the experimental set-up .



RESULTS

I) ANGII induced CVD does not impact LLC tumor growth

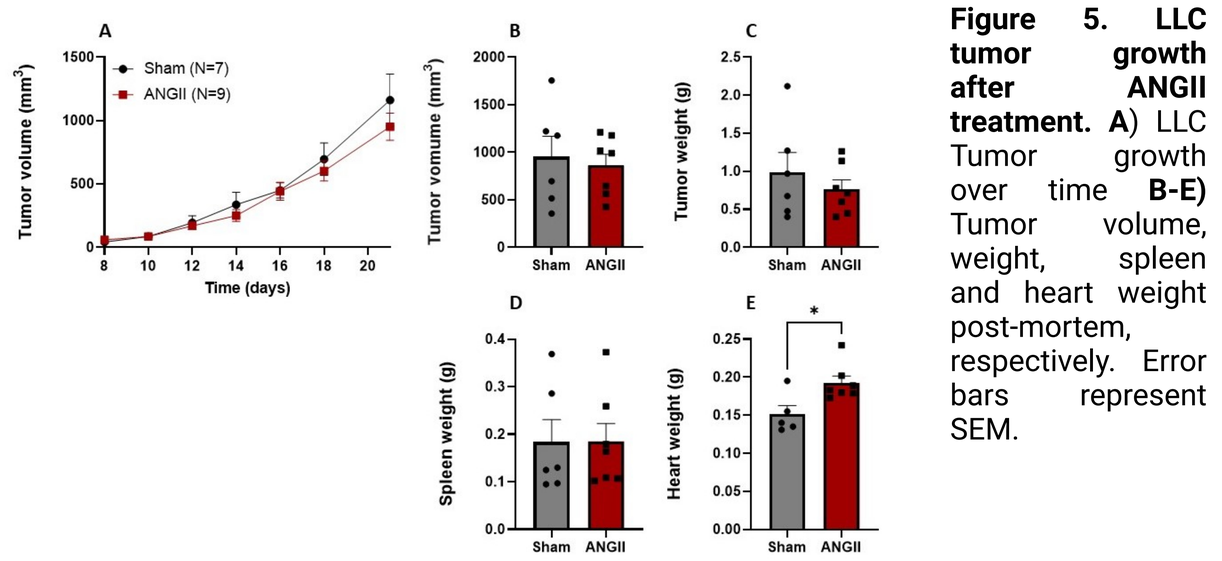
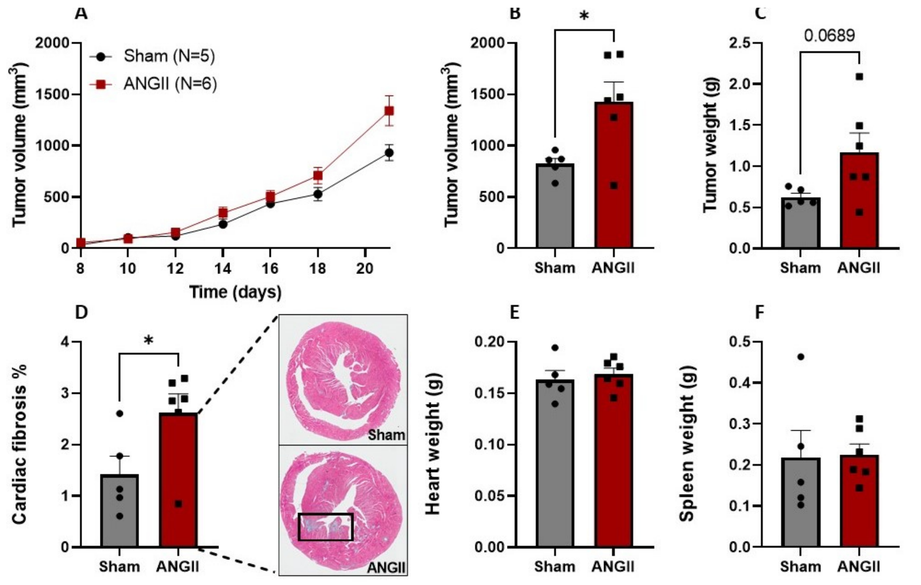


Figure 5. LLC tumor growth after ANGII treatment. A) LLC Tumor growth over time **B-E)** Tumor volume, weight, spleen and heart weight post-mortem, respectively. Error bars represent SEM.

II) ANGII directly impacts LLC growth

Figure 6. LLC tumor growth concomitantly with ANGII treatment. A) LLC tumor growth over time **B-F**) Tumor volume and weight, Cardiac fibrosis, heart and spleen weight, respectively. error bars represent SEM.



III) ANGII increases polyp count in SI of APC- mice

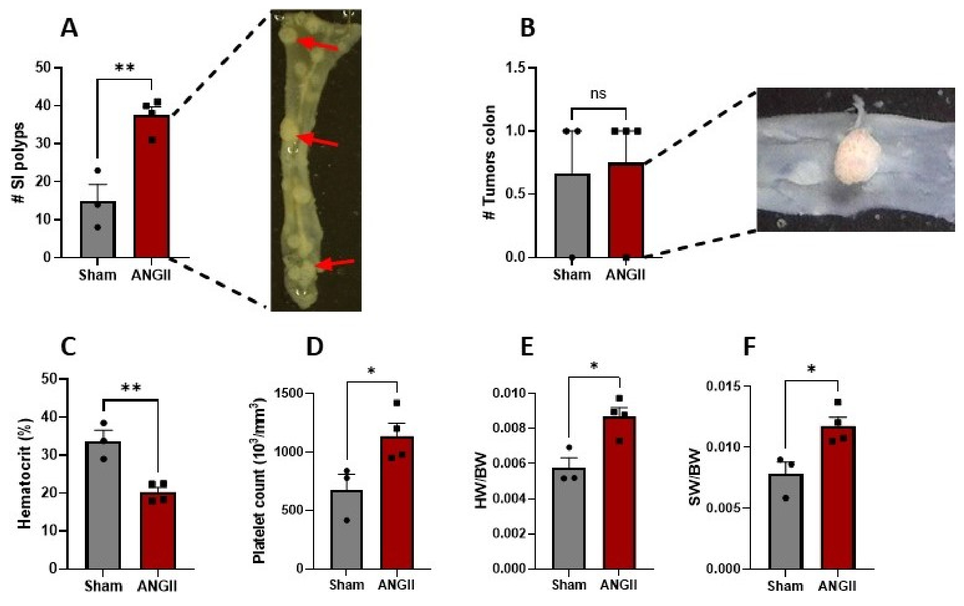


Figure 7. Effect of ANGII on APC- tumor growth. A-B) Polyp and Tumor count in the SI and colon, respectively. **C-F)** Hematocrit value, platelet count , HW/BW and SW/BW ratio, respectively. Error bars represent SEM.

CONCLUSION

ANGII directly enhances LLC tumor growth and increased APC- polyp count. This suggests a role for ANGII in CVD-enhanced cancer growth. Although further investigation is required to unravel the role of ANGII, screening cancer patients with CVD comorbidities for ANGII involvement might be warranted.

Contact information:

benji.vanberlo@uantwerpen.be

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