

Immunomodulation as a tool to fight cancer cachexia and sarcopenia in the elderly

Noviello C.*^{a,b}, Iaia N.*^{a,b}, Genta B.*^b, Rubini G.^b, Penna F.^b and Costelli P.^b

*equally contributed

^a Dept. of Translational Medicine, University of Eastern Piedmont, Italy

^b Dept. of Clinical and Biological Sciences, University of Turin, Italy



UNIVERSITÀ DI TORINO



INTRODUCTION

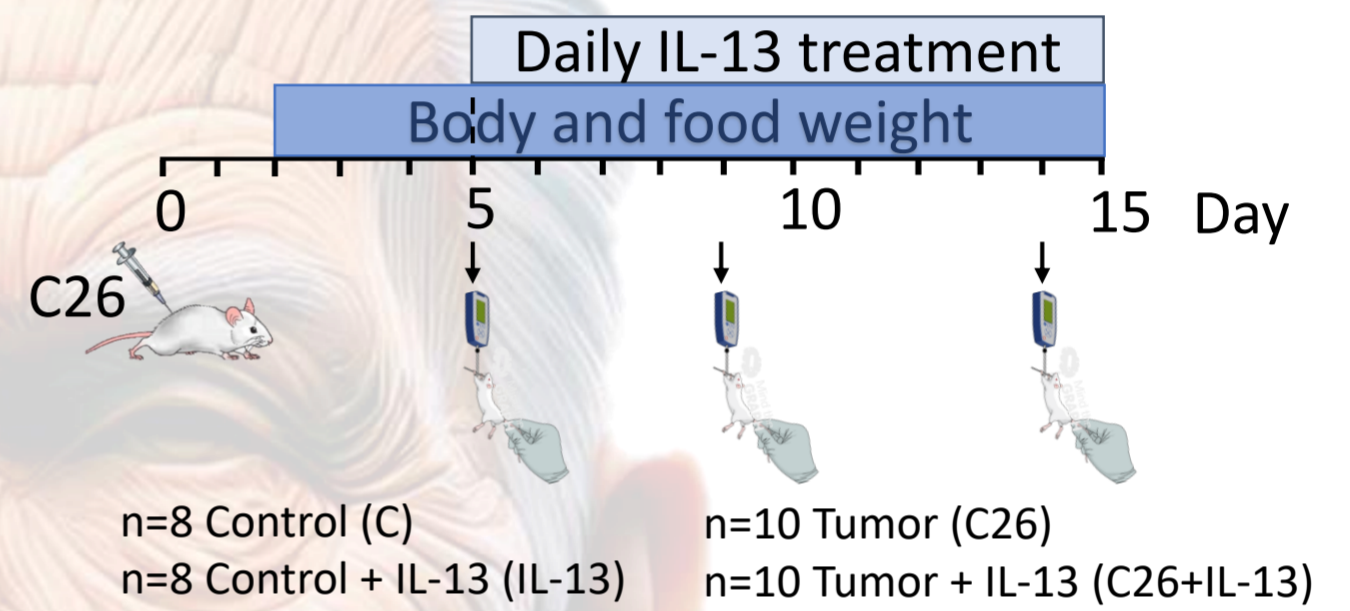
Worldwide population average age is enormously rising. However, a longer life expectancy increases the risk of developing conditions that compromise the prospect of healthy aging, such as sarcopenia, which causes the loss of muscle mass and function. Increasing age is also associated with a higher probability to develop cancer. Cancer patients are frequently affected by cachexia, a multifactorial syndrome that manifests as involuntary body weight loss and progressive decline in skeletal muscle mass. Therefore, it is very difficult to treat elderly cancer patients developing cancer cachexia having an already compromised skeletal muscle homeostasis. Recently, both cachexia and ageing have been associated with an altered systemic inflammatory response. Previous observations showed that administration of interleukin (IL)-4 to the C26-bearing mice improved cachexia preserving muscle function. In the same experimental model, a significant reduction in both mRNA and protein levels of IL-13 has been detected (Costamagna et al. 2020). This cytokine has been defined as essential for the metabolic adaptation that takes place in the muscle after endurance exercise (Knudsen et al. 2020).

AIM

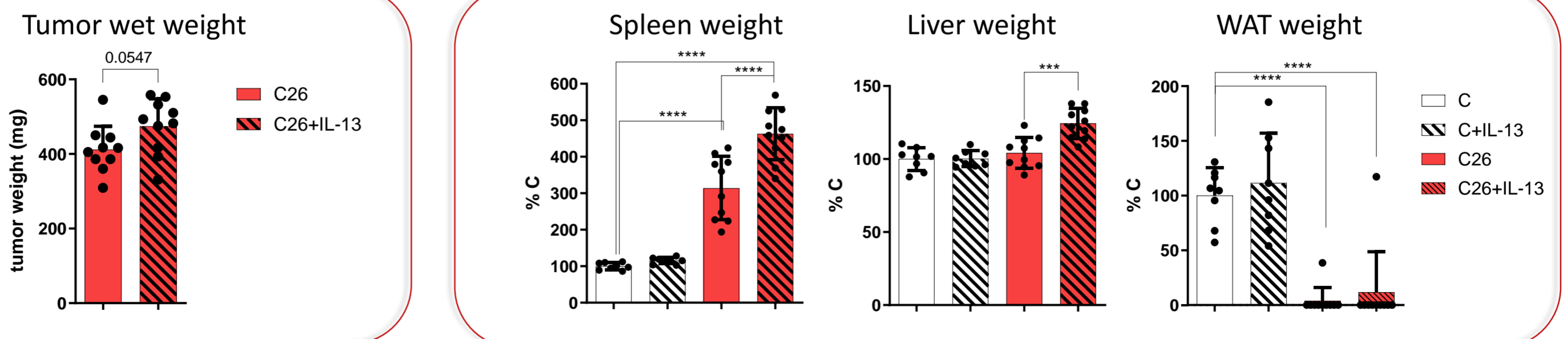
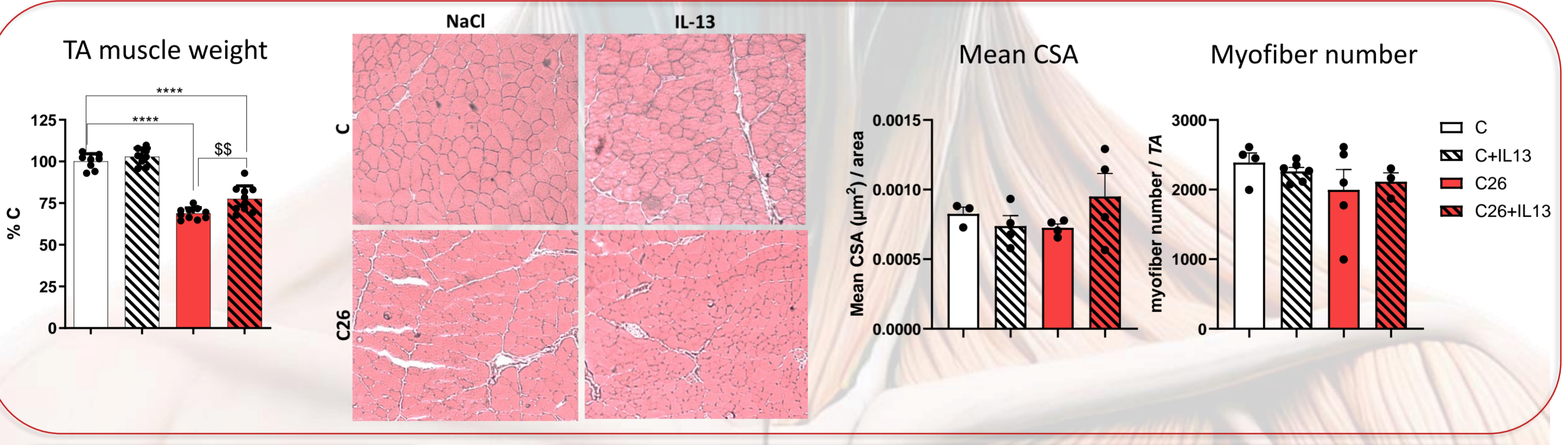
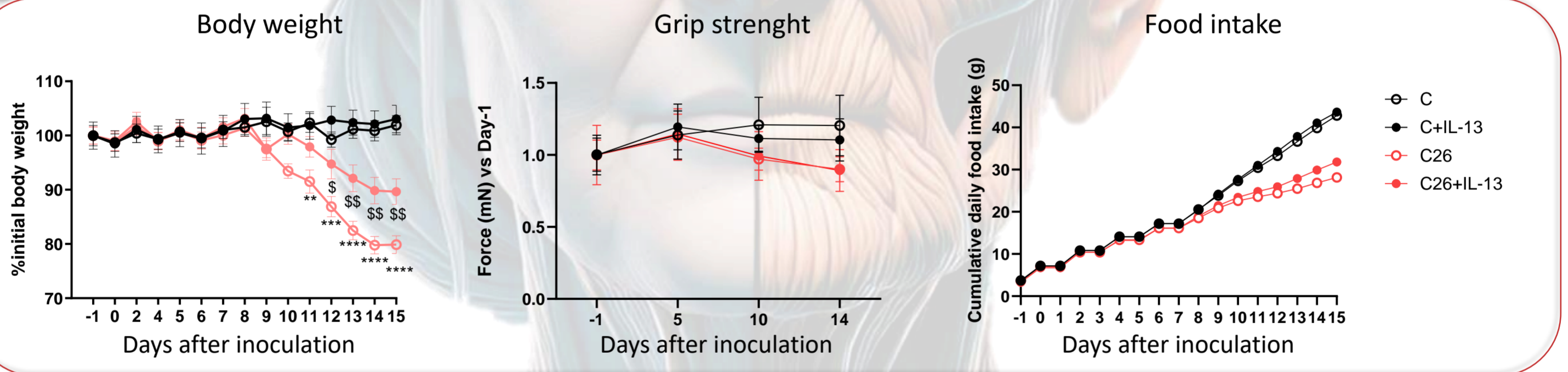
To investigate whether IL-13 administration is relevant for muscle homeostasis during experimental cancer cachexia.

METHODS

Ten-weeks old Balb/c male mice were subcutaneously inoculated with 5×10^5 C26 colon carcinoma cells. Five days after the inoculation, IL-13 was administered daily intraperitoneally (1,5 $\mu\text{g}/\text{mouse}$) until the day of sacrifice. The control groups received intraperitoneal injection of physiological solution. Body weight, food intake and muscle grip strength were evaluated. On the day of sacrifice, muscles and organs were collected, weighed and stored for further analyses.



RESULTS



Significance of the differences: ** $p < 0.01$, **** $p < 0.0001$ vs C; \$ vs C26

CONCLUSIONS

Our preliminary data suggest that IL-13 treatment may have a positive impact on cancer cachexia, due to its ability to limit body weight loss and muscle mass reduction in tumor-bearing mice. Furthermore, IL-13 treatment induces spleen and liver enlargement, suggesting an impact on the immune response. Considering that muscle wasting also characterizes aging, anti-inflammatory strategies based on IL-13 exposure could be investigated as tools useful to improve sarcopenia in elderly people as well, in the presence or in the absence of cancer.