Cardiac expression of NGAL is up-regulated in experimental cancer cachexia

V. Musolino[1], M. Gliozzi[1], C. Carresi[1], C. Giancotta[1], A. Scarcella[1], F. Scarano[1], F. Oppedisano[1], J. Maiuolo[1], A. Maretta[1], L.A. Giancotti[1], F. Lauro[1], S. Ilari[1], E. Palma[1], C. Muscoli[1], J. Springer[2], S.D. Anker[2], V. Mollace[1]

[1]Institute of Research for Food Safety & Health (IRC-FSH), University of Catanzaro
[2]Division of Innovative Clinical Trials, Dept. of Cardiology, University Medical Center Göttingen (UMG), Göttingen, Germany

NGAL is commonly seen as a marker of kidney injury; however, it has also been associated with critically ill patients (heart failure, sepsis, multi-organ failure) and is thought to play a role in cancer cell motility. Here we compared the mRNA expression of NGAL in the heart of cachetic rats bearing the Yoshida hepatoma (n=16) to that of the aldosterone antagonist spironolactone-treaded (5 or 50 mg/kg/d, n=11 and 9, respectively) rats as well as healthy controls (n=10). Plasma levels of NGAL and aldosterone were assessed by ELISA.

Tumor bearing rats lost 45±4g body weight, while controls gain 61±3g ($p<0.001$) after 16 days. Five mg/kg/d spironolactone reduced wasting (-25±10g) and 50mg/kg/d stopped weight loss (+0.5±16g, both $p<0.05$). Cardiac NGAL mRNA expression was up-regulated by 93% compared to controls ($p<0.05$) and was reduced to control levels by 50 mg/kg/d spironolactone ($p>0.05$), while the 5mg/kg/d dose was not effective. Aldosterone was up-regulated from 337±7 pg/mL in controls to 591±31 pg/mL in the placebo group ($p<0.001$) and reduced to 396±22 pg/mL in animals treated with 50mg/kg/d spironolactone ($p<0.01$). Plasma levels of NGAL were increased in tumor-bearing rats (1462±360 g/L) compared to controls (93±6 g/L, $p<0.001$). High dose spironolactone reduced NGAL levels to 530±77 g/L ($p<0.05$ vs placebo). Cardiac function assessed by echocardiography was markedly improved by high dose spironolactone. Cardiac output on day 11 was decreased in the placebo group compared to control 49±7 mL/min vs 80±7 mL/min, respectively $p<0.01$). This functional impairment was reduced by high dose spironolactone (79±7mL/min, $p<0.01$ vs placebo), which may functionally reflect the reduction of NGAL mRNA in the heart and protein in plasma. This may suggest that NGAL could potentially be used as a biomarker to assess cardiac impairment in cancer cachexia. However, more studies are needed to confirm our results.