Abstract 76

Gut microbiome metagenomic analysis identifies key functional pathways associated with sarcopenia development in patients with metastatic renal cell carcinoma

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BACKGROUND

- Sarcopenia, or the loss of skeletal muscle mass, is associated with poorer clinical outcomes among patients with various cancers (Shachar *et al., Eur J Cancer*, 2016).
- In this study, we explored the relationship between the gut microbiome and metabolome signatures and sarcopenia among individuals diagnosed with metastatic renal cell carcinoma (mRCC).

METHODS

- mRCC patients who had stool whole metagenome sequencing as part of institutional research studies were retrospectively identified.
- Patients with CT imaging prior to the stool sample collection were identified and L3 axial segment muscle mass area (MMA) was calculated (sliceOmatic, TomoVision, Canada).
- Sarcopenia status was determined by using previously published gender and body mass index based skeletal muscle index (MMA/height^2) cutoffs (Mourtzakis *et al., Appl Physiol Nutr Metab*. 2008).
- Taxonomy profile was generated with MetaPhlAn 3.0. Differentially abundant species and metabolic pathway expression were identified with LDA effect size analysis and HUMAnN 3.0, respectively.

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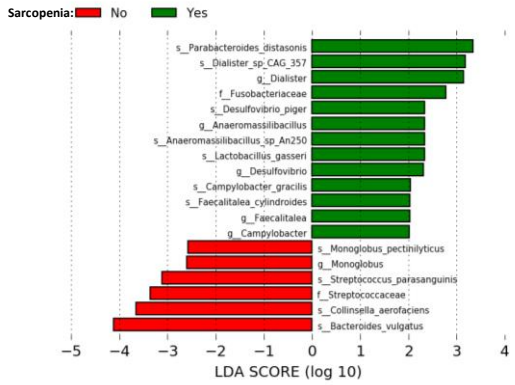
RESULTS

Table 1. Patient characteristics

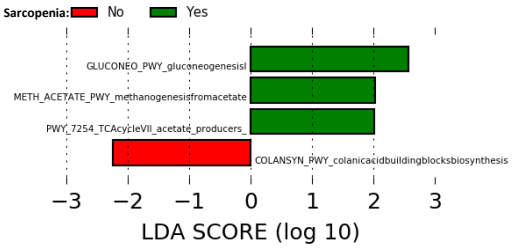
Number of patients	62
Median age, years (range)	69 (33-93)
Gender – no. (%)	
Female	17 (27.4)
Male	45 (72.6)
Race – no. (%)	
White	53 (64.6)
Asian	8 (9.8)
Unknown	1 (1.2)
ECOG performance status	
0	46 (74.2)
1	12 (19.4)
≥2	5 (4.8)
BMI – mean (SD)	26.7 (5.6)

Figure 1. Differentially expressed species



- Species that were differentially abundant with an LDA score three and above in sarcopenic patients (n=27) were *Parabacteriodes distasonis, and Dialister sp CAG 357,* whereas in non-sarcopenic patients (n=35), *Bacteriodes vulgatus, Colinsella aerofaciens, and Streptococcus parasanguinis* were more abundant.

Figure 2. Functional pathway analysis



Functional Pathway	Sarcopenia	P-value
Colanic acid building blocks biosynthesis	No	0.032907
Gluconeogenesis I	Yes	0.008652
Methanogenesis from acetate	Yes	0.040825
TCA cycle VII acetate producers	Yes	0.040698

- Sarcopenic patients were enriched in pathways involved in gluconeogenesis I, methanogenesis from acetate and TCA cycle VII pathways. Whereas, in non-sarcopenic patients, colonic acid or M antigen synthesis pathway expression were enriched.

CONCLUSION

- This is the first study examining the association between sarcopenia and metabolic expression of the gut microbiome in patients with mRCC.
- We observed an increased expression in the gluconeogenesis related pathways in patients with sarcopenia suggesting a potential catabolic state of the host.