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B032

Cancer cachexia marker, Growth Differentiation Factor 15 (GDF-15), serum level mapping in real world samples from patients with pancreatic (PANC) or colorectal cancer (CRC)

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Objective

- This study evaluated circulated GDF-15 levels in real-world clinical samples from patients with CRC or PANC, diagnosis and explored correlations with demographic and clinical parameters

Conclusions

- Elevated circulating GDF-15 levels correlated positively with age; there was a trend towards higher GDF-15 levels with advanced disease stage and in males in both CRC and PANC, consistent with prior studies[1]
- Smoking status correlations were inconclusive

Limitations

- This is an observational study with real-world patient data. The findings of GDF-15 levels should be interpreted in the appropriate context of a naturally imbalanced study population
- Results are based on a limited dataset and validation in a large real-world dataset is needed to investigate the role of baseline circulating GDF-15 values in different tumor types and in cancer related cachexia/anorexia (CRCA)

Background: Cancer Related Cachexia/Anorexia and GDF-15

- **CRCA a multifactorial syndrome,** is a common cancer comorbidity and critical unmet need characterized by loss of appetite, unintentional weight loss and skeletal muscle loss, leading to fatigue, functional impairment, increased treatment related toxicity, poor quality of life, and reduced survival[2,3,4]
- **GDF-15** an inflammatory cytokine, is present in healthy subjects at low levels; higher GDF-15 levels are associated with CRCA in multiple tumor indications and other disease states. GDF-15 has emerged as a potential therapeutic target for CRCA, and mapping of circulating GDF-15 levels to disease severity in different tumor indications is important to understand how GDF-15 contributes to the CRCA phenotype[2,3,5]

Methods

- Commercial serum samples and associated demographics and tumor characteristics from patients with CRC or PANC (n=100 from USA [n=83], Ukraine [n=17]) were obtained (BioIVT, Woodbury, NY) (**Table 1**)
- Serum was analyzed using an electrochemiluminescence immunoassay developed and validated to quantify GDF-15 in human serum using a custom anti-GDF-15 antibody (AVEO Pharmaceuticals, Inc., Boston, MA) as capture reagent and human GDF-15 antibody (R&D Systems, Minneapolis, MN) as detection reagent. Recombinant human GDF-15 (R&D Systems, Minneapolis, MN) was used as a positive control. Assay sensitivity was 48.7 pg/mL in human serum.
- Descriptive statistics for GDF-15 circulating levels were presented by cancer type, gender, age, disease stage, and smoking status.

Results

Table 1. Patient Demographics

	Overall Study Population N=100	
Cancer Type	CRC N (%)	PANC N (%)
	56 (56%)	44 (44%)
Age		
<45	3 (5.4%)	1 (2.3%)
45-65	21 (37.5%)	11 (25%)
>65	31 (55.4%)	30 (68.2%)
Unknown	1 (1.8%)	2 (4.5%)
Disease Stage		
Stage I/II	7 (12.5%)	14 (31.8%)
Stage III	31 (55.4%)	7 (15.9%)
Stage IV	13 (23.2%)	18 (40.9%)
Unknown	5 (8.9%)	5 (11.4%)
Gender		
Male	32 (57.1%)	22 (50%)
Female	22 (39.3%)	22 (50%)
Smoking Status		
Smokers (current or previous)	9 (16.1%)	12 (27.3%)
Non-smokers	20 (35.7%)	21 (47.7%)
Unknown	27 (48.2%)	11 (25%)

Table 2. GDF-15 Levels (pg/mL) in CRC and PANC

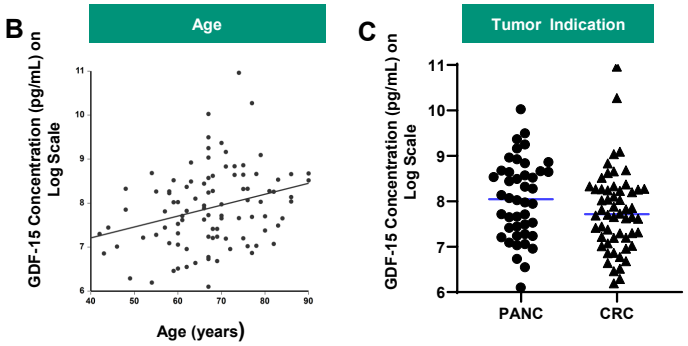
Cancer Type	CRC				PANC			
	N (%)	Median	Min	Max	N (%)	Median	Min	Max
	56	2240	490	>57600*	44	3120	446	22600
Disease Stage								
Stage I/II	7 (12.5%)	1470	765	28900**	14 (31.8%)	3415	699	13300
Stage III	31 (55.4%)	2110	490	8890	7 (15.9%)	1390	1130	7050
Stage IV	13 (23.2%)	3090	639	>57600*	18 (40.9%)	5470	446	22600
Unknown	5 (8.9%)	3880	539	5760	5 (11.4%)	1790	1660	4110
Gender								
Male	32 (57.1%)	2575	539	28900**	22 (50%)	4755	446	13300
Female	22 (39.3%)	1870	490	>57600*	22 (50%)	2235	699	22600
Smoking Status								
Smokers (current/previous)	9 (16.1%)	3070	875	4310	12 (27.3%)	1945	446	7790
Non-smokers	20 (35.7%)	2145	490	>57600*	21 (47.7%	5010	1050	22600
Unknown	27 (48.2%)	2110	539	28900**	11 (25%)	3190	1130	10400

Footnote: Higher GDF-15 levels reported in patients with co-morbidities like thalassemia (*) & Parkinson's (**). Six patients had diagnosed anorexia, 1 CRC (1500pg/mL) and 5 PANC (1130-7500 pg/mL), 3 additional patients (2 CRC and 1 PANC) were reported to have abnormal weight loss (3630- >57600 pg/mL).

Figure 1. GDF-15 Correlation with Age (A, B) or Tumor Indication (C)

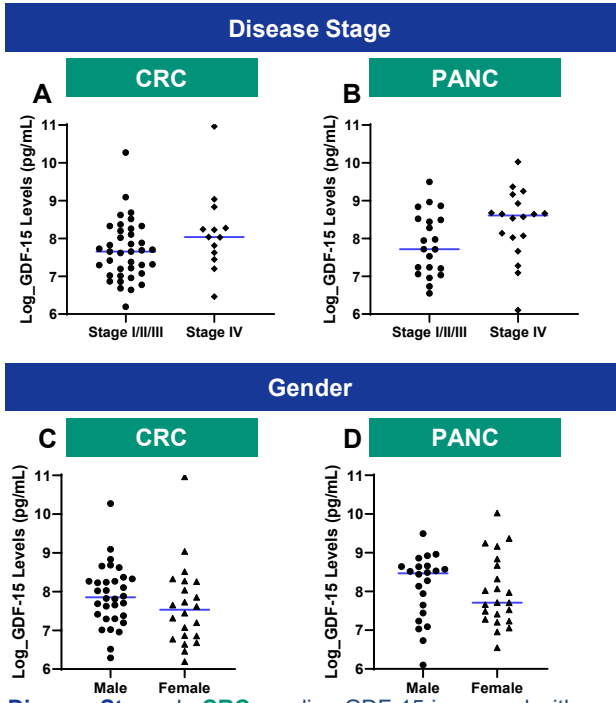
A

Age	GDF-15 Levels (pg/mL)	
	N (%)	Median (Range)
<45 years	4	1475 (950 - 1710)
45-65 years	32	2130 (490 - 7500)
>65 years	61	3090 (446 - >57600)
Unknown	3	3630 (2100 - 7790)



Univariate analysis of GDF-15 levels (on natural log scale) with age showed a moderate positive correlation (Figure 1A, B, Pearson correlation coefficient: 0.3; *p-value*= 0.0028). The solid line represents the linear regression slope. Although median GDF-15 value (blue line) appears higher in PANC compared with CRC (Figure 1C), the difference was not statistically significant.

Figure 2. Evaluation of Correlation between GDF-15 and Disease Stage (A, B), and Gender (C,D)



Disease Stage: In **CRC**, median GDF-15 increased with advancing disease stage (**Figure 2A, Table 2**). In **PANC,** median GDF-15 was higher in patients with Stage IV disease compared to Stage I/II, or Stage III (**Figure 2B, Table 2**). **Gender and Smoking Status:** Males had a higher median GDF-15 vs females in both CRC and PANC (**Figure 2C,D, Table 2**). Higher GDF-15 correlated with smoking in CRC but non-smoking in (**Table 2**), and in males vs. females (**Figure 2D, Table 2).** A statistical significance could not be achieved for these differences. Blue lines represent the median values.

References: [1]Hüllwegen et al., Trends Cancer. 2025; [2]Fearon et al., *Nat. Rev. Clin. Oncol*. 2013; 10:90-99; Jul 9:S2405-8033(25)00150-5; [3]Lerner et al., *J. Cachexia Sarcopenia Muscle*. 2015; 6:317-324; [4]Roeland et al., *J. Clin. Oncol*. 2020; 38:2438-2453; [5]Roeland et al., *J Clin Oncol. 2025;* 43, 12060