Multi-omic characterization of RCC1 expression and its association with molecular alterations, immune phenotypes, and cancer outcomes

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Background
- Regulator of Chromosome Condensation 1 (RCC1) is the only identified guanine nucleotide exchange factor for Ras-related nuclear protein Ran and it functions in the control of chromosome condensation and telomere positioning.
- RCC1 is a positive regulator of chromosome condensation and telomere positioning, and is associated with poor outcomes.

Methods
- DNA (SSG-gene or whole exome) and RNA (whole transcriptome) sequencing was performed at Caris Life Sciences.
- Immune analysis was performed using a panel of 40 immune-related genes.

Results
- RCC1 expression is associated with poor outcomes across several cancer types.
- RCC1 expression is a negative prognostic factor across several cancer types.
- RCC1 expression is associated with immune phenotypes and cancer outcomes.
- High RCC1 expression was associated with increased dendritic cell (DCT) and reduced CD8+ and Treg fractions.

Conclusions
- RCC1 expression is a negative prognostic marker in NSCLC, PC, and CRC.
- Further studies to investigate this at the molecular level may be a potential opportunity for novel targeted drug development.

References
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Figure 1. Box-and-whisker plot of RCC1 expression by cancer type lineage. Median RCC1 expression highest in SCCL (Q1–Q3 TP5M), followed by GC (Q1–Q3), NSCLC (Q1–Q3), CRC (Q1–Q3), and PC (Q1–Q3).

Figure 2. Frequency of immunotherapy-related biomarkers by cancer type.

Figure 3. Estimation of infiltrating immune cell fractions by RCC1 expression quartiles.

Figure 4. High RCC1 expression was associated with worse OS in NSCLC (HR 1.3*), PC (HR 1.52*, P<0.00001), and CRC (HR 1.979, P=0.252), with a similar but not significant effect in SCLC (HR 1.2, P<0.0001).

Table 1 and 2. Relative frequency of biomarker alterations between RCC1 Q1 and RCC1 Q4 expression subgroups. Positive values in red indicate higher frequency in RCC1 Q4, and negative values in blue indicates higher frequency in RCC1 Q1. In PC, TP53 mutations (Q1–Q4 range: 70-81%/1) and MYC amplifications (1-4%) were more frequent among RCC1 Q4, whereas ATM mutations were less frequent (6-3%). In CRC, TP51 (Q1–Q4 range: 70-81%) and KPI (Q1–Q4 range: 70-81%) mutations were more frequent in RCC1 Q4, while GNAS mutations were less frequent (4-2%).

Figure 4. High RCC1 expression was associated with worse OS in NSCLC (HR 1.3*), PC (HR 1.52*) and CRC (HR 1.979), with a similar but not significant effect in SCCL (HR 1.2) and GC (HR 1.1).