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Characterisation of distinct molecular phenotypes in high-grade serous ovarian cancer biopsies to predict neoadjuvant chemotherapy response

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Introduction/Aims

Neoadjuvant chemotherapy (NACT) response in advanced ovarian cancer (AOC) is highly heterogeneous.
The COBIOPRED project aims to identify transcriptomic signatures in pre-treatment biopsies that predict the Chemotherapy Response Score (CRS).

Methodology

RNA-seq was performed on 54 pre-NACT biopsies (18 CRS1, 20 CRS2, 16 CRS3). Unsupervised hierarchical clustering and differential expression analysis identified gene sets and molecular niches associated with chemo-sensitivity.

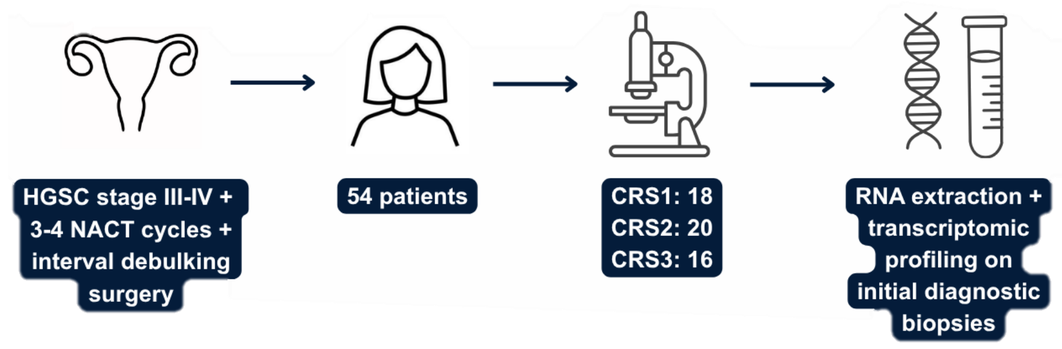

Figure 1. Study design and cohort selection workflow.

Results

Distinct signatures stratified patients. Excellent responders (CRS3) overexpressed ADAM23, PTCH1, ROBO2, ESR2 and PAX2, suggesting a differentiated, hormonally regulated phenotype. Poor responders (CRS1) showed upregulation of SYNE4 and THRB-IT1. The combined CRS1/2 group exhibited a PADI3, EYA4 and TSPAN1 overexpression. PLTP upregulation in these resistant niches suggest M2-macrophage polarisation and immune evasion as drivers of NACT failure.

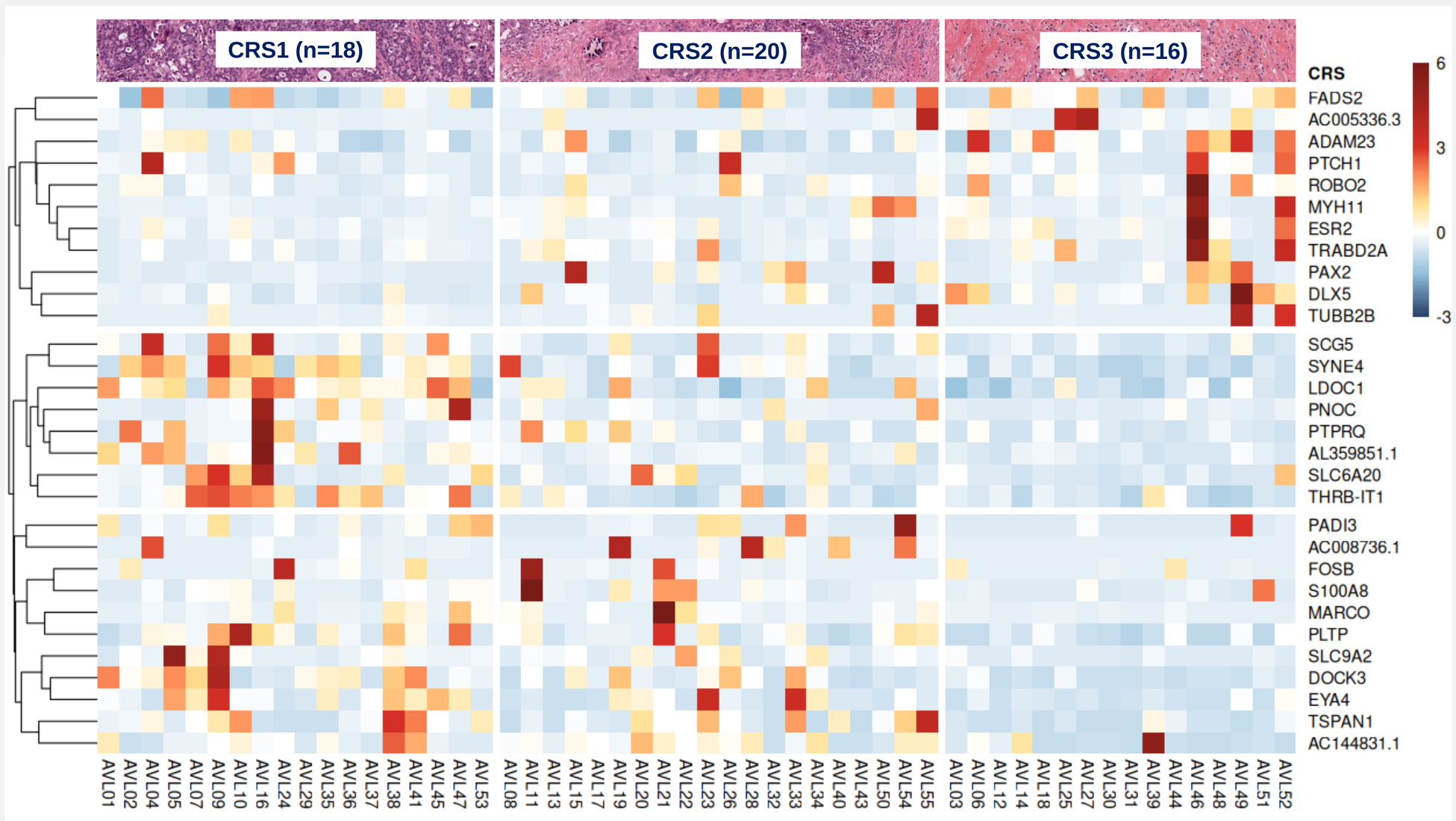

Figure 2. Gene expression across CRS groups.
Heatmap showing normalized gene expression levels in pre-treatment ovarian cancer biopsies stratified by CRS
Rows represent genes and columns represent individual samples.
Expression values are displayed as row-scaled Z-scores relative to normal tissue (red=higher expression, blue= lower expression

	CRS1/2	CRS3
Biological phenotype	Less differentiated, pro-tumorigenic	Differentiated, hormonally regulated
Key upregulated genes	SYNE4, PADI3, EYA4, TSPAN1, PLTP	ADAM23, PTCH1, ROBO2, ESR2, PAX2
Functional profile	Cell growth, invasion, cytoskeletal organization	Tumour suppression, differentiation, hormone signaling
Tumour microenvironment	Pro-tumorigenic niche with immune modulation	Less prominent pro-tumorigenic signaling
Immune context	Suggestive of M2 macrophage polarization and immune evasion	Not specifically enriched

Table 1. Comparative transcriptomic features between CRS1/2 and CRS3 groups

Conclusion

These preliminary findings suggest CRS categories represent divergent biological entities. This exploratory study provides a basis for a **candidate molecular signature to predict NACT efficacy** from initial biopsies.

While requiring validation, these results represent a first step toward identifying biomarkers to guide **personalised surgical decisions** (primary cytoreduction vs. NACT + interval debulking surgery), potentially optimising clinical outcomes and minimising comorbidities in AOC.

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References