

#3566: Sensitizing potential of a novel stimulated and hapttenized vaccine in immunotherapy-resistant metastatic colorectal cancer

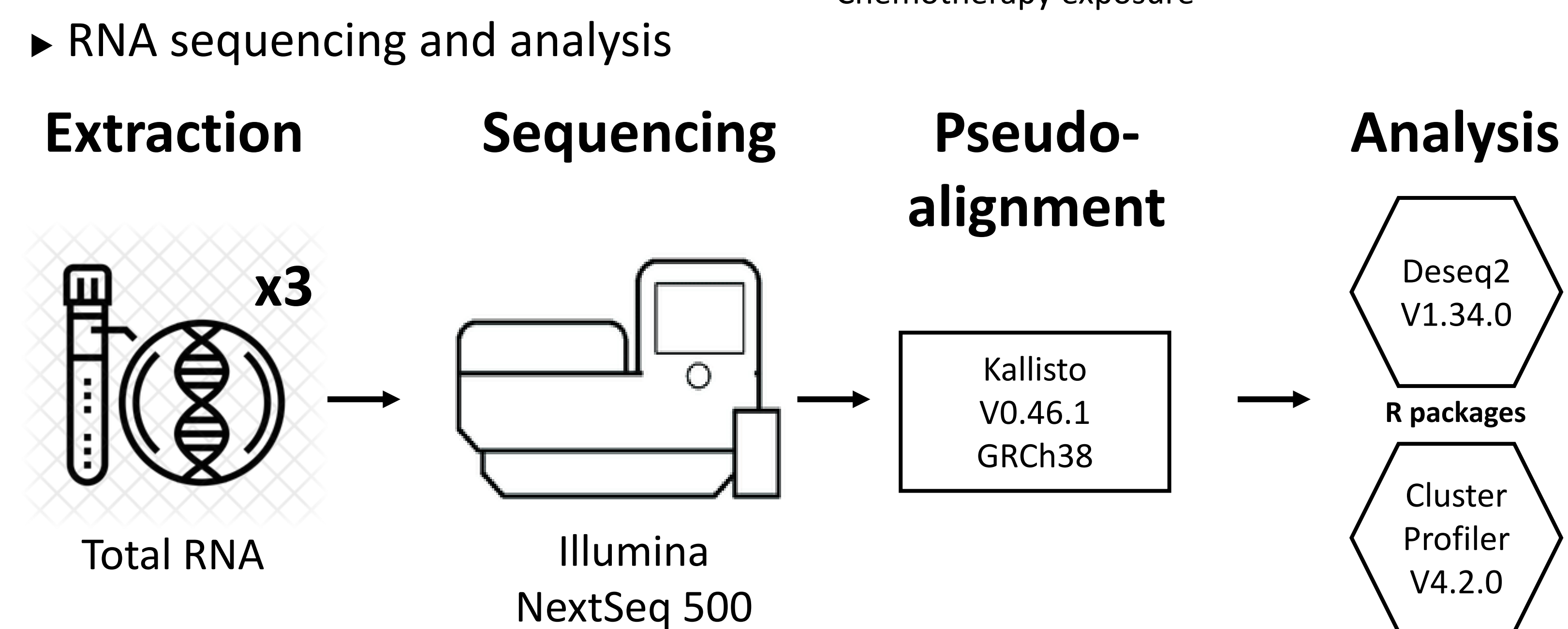
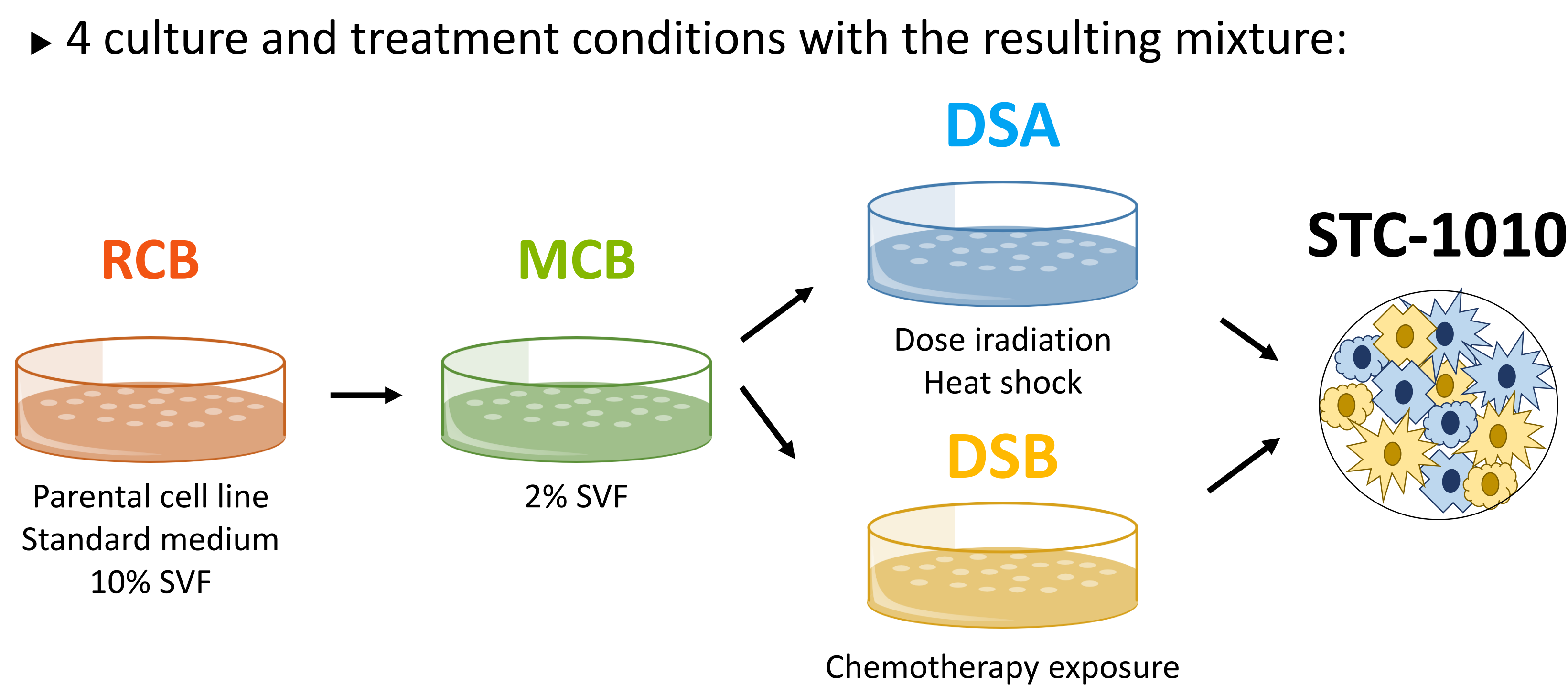
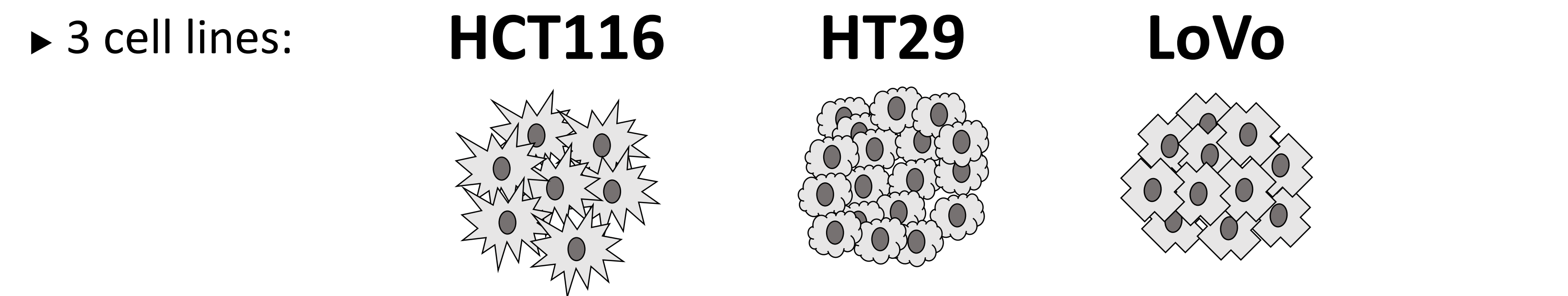
Corentin RICHARD, Sandy CHEVRIER, Lionel CHALUS, Jeremy FORGET, Benoît PINTEUR, Paul BRAVETTI and Romain BOIDOT

INTRODUCTION

- Colorectal cancer (CRC) is the second most common solid organ cancer.
- The relative therapeutic resistance of these tumors to I/O drives the need for new treatments.
- STC-1010 therapeutic vaccine (Brenus Pharma) is composed of selected tumor cell lines, stimulated to overexpress TAA/TSA and neoantigens including resistant factors that are further hapttenized.
- The formed immunogenic haptten-protein complex could potentially educate the immune system to recognize and target the patient's tumor cells expressing the same resistance factors.

We report the transcriptomic changes induced by the different treatment and culture conditions on each cell line.

STUDY DESIGN AND METHODS



WHOLE-TRANSCRIPTOME PROFILING

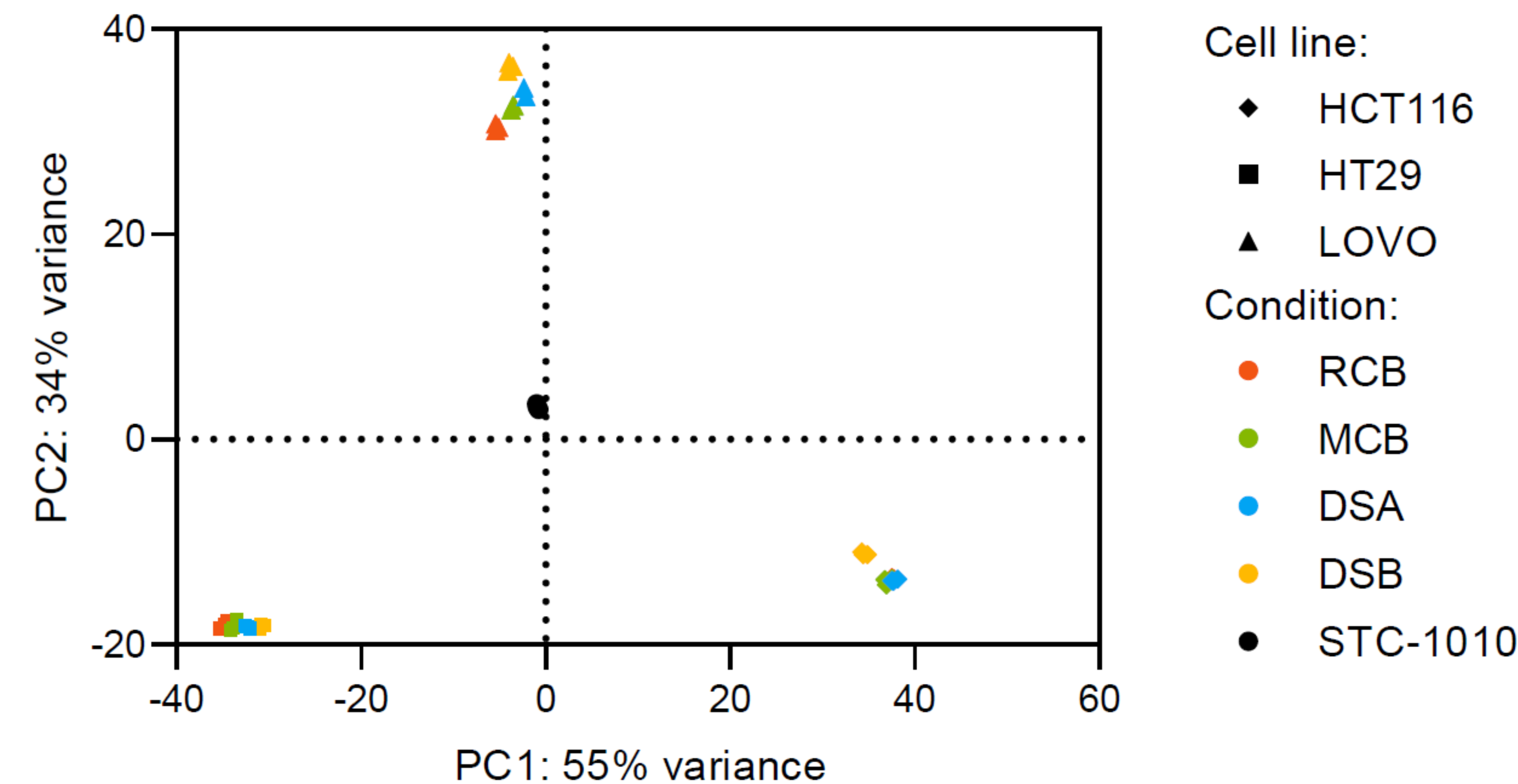


Figure 1: Principal component analysis of the whole-transcriptome.

- Conditions do not affect the transcriptome of the 3 cell lines in the same way.
- STC-1010 displays a balanced transcriptomic profile.

DIFFERENTIAL ABUNDANCE ANALYSIS

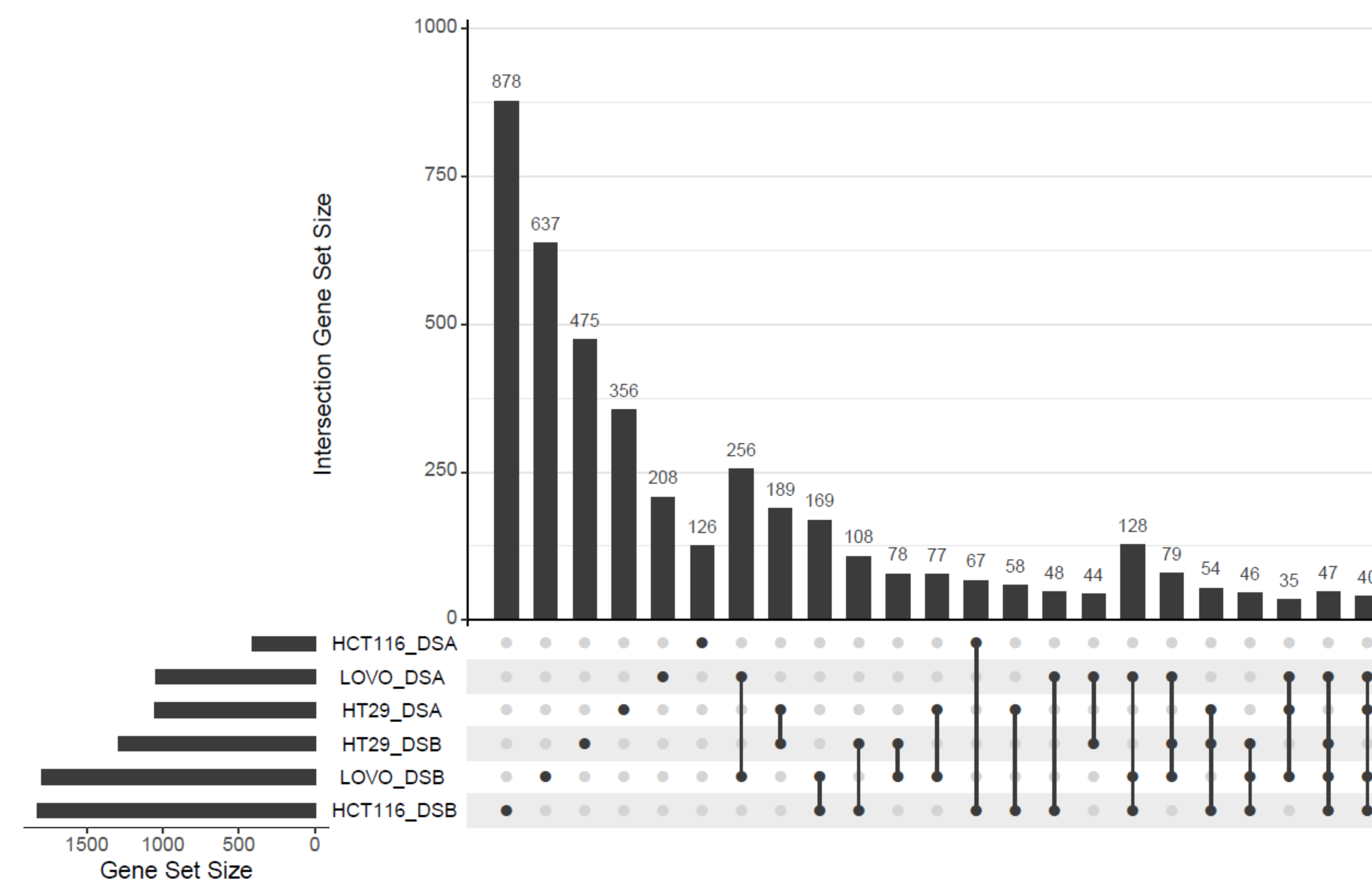


Figure 2: Upset plot of differentially expressed genes across MCB versus DSA and DSB comparisons for each cell line.

- The conditions do not affect the same genes for the 3 cell lines.
- Few common genes, transcriptomes are specifically modulated.

GENE SET ENRICHMENT ANALYSIS

Table 1: GSEA analysis for MCB versus DSA and DSB comparisons (KEGG db).

Pathway	HCT116		HT29		LoVo	
	DSA	DSB	DSA	DSB	DSA	DSB
Base excision repair	↗		↗	↗		
Cell cycle		↘	↗	↗	↘	↘
DNA replication	↗	↘	↗	↗	↘	↘
Homologous recombination	↗		↗	↗		
Human papillomavirus infection		↗		↗	↗	↗
Mismatch repair	↗		↗	↗		
Nucleotide excision repair	↗		↗	↗		
p53 signaling pathway	↗	↗		↗	↗	↗
Allograft rejection		↗				
Antigen processing and presentation	↗					
Graft-versus-host disease						↗
Natural killer cell mediated cytotoxicity						↗
Neutrophil extracellular trap formation		↘	↗	↘	↘	↘
Proteasome	↗		↗		↘	↘
Protein export	↗				↘	↘
Protein processing in endoplasmic reticulum	↗				↘	↘
TGF-beta signaling pathway	↘					
TNF signaling pathway	↘				↗	↗
Viral protein interaction with cytokine		↗	↘		↗	↗

- Impact on genes involved in
 - DNA repair pathways,
 - Antigen processing and presentation,
 - Immune system modulation pathways.
- Complementarity between the different cell lines and conditions.

CONCLUSION

Brenus STC vaccine based on physical and chemical stimulations and hapttenization reveals a promising potential to sensitize MSS CRC immunotherapy-resistant tumors to immune checkpoint inhibition therapy. Further studies are ongoing to profile and analyze the proteosurfaceome of each cell line.

Corentin Richard, PhD
 Centre Georges-François Leclerc
 1 rue Professeur Marion, Dijon, France
crichard@cgfl.fr

