



LUND UNIVERSITY

Copy number signatures for early diagnosis of high-grade serous ovarian carcinoma

Martin de la Fuente, Laura; Li, Minerva; Måsbäck, Anna; Malander, Susanne; Kannisto, Päivi; Hedenfalk, Ingrid

2022

[Link to publication](#)

Citation for published version (APA):

Martin de la Fuente, L., Li, M., Måsbäck, A., Malander, S., Kannisto, P., & Hedenfalk, I. (2022). *Copy number signatures for early diagnosis of high-grade serous ovarian carcinoma*. Poster session presented at "FUTURE PERSPECTIVES IN OVARIAN CANCER RESEARCH", Stockholm, Sweden.

Total number of authors:

6

Creative Commons License:

Unspecified

General rights

Unless other specific re-use rights are stated the following general rights apply:

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

Read more about Creative commons licenses: <https://creativecommons.org/licenses/>

Take down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

LUND UNIVERSITY

PO Box 117
221 00 Lund
+46 46-222 00 00

Copy number signatures for early diagnosis of high-grade serous ovarian carcinoma

BY LAURA MARTIN DE LA FUENTE¹, MINERVA X. LI¹, ANNA MÅSBÄCK², SUSANNE MALANDER¹, PÄIVI KANNISTO³, SRINIVAS VEERLA¹ AND INGRID HEDENFALK¹

¹DEPARTMENT OF CLINICAL SCIENCES LUND, DIVISION OF ONCOLOGY, LUND UNIVERSITY AND SKÅNE UNIVERSITY HOSPITAL, LUND, SWEDEN.

²DEPARTMENT OF SURGICAL PATHOLOGY, DIVISION OF LABORATORY MEDICINE, SKÅNE UNIVERSITY HOSPITAL, LUND, SWEDEN.

³DEPARTMENT OF OBSTETRICS AND GYNAECOLOGY LUND, SKÅNE UNIVERSITY HOSPITAL, LUND UNIVERSITY, LUND, SWEDEN.

Background

The detection of ovarian carcinoma-derived somatic mutations in cervical samples and uterine lavages in several studies since 2013, has brought hope for the development of new biomarkers for early detection. High-grade serous ovarian carcinoma (HGSC) is strongly dominated by copy number alterations (CNAs). These CNAs are the consequence of underlying mutational processes in HGSC. We interrogated CNAs from low coverage whole-genome sequencing (WGS) data in HGSC tumors, plasma, endometrial biopsies, and cervical samples to explore if copy number signatures can be used as a biomarker for early detection of HGSC.

Methods

A total of 204 samples were included from 18 patients with HGSC, four *BRCA* mutation carriers and seven benign controls. Estimations of ploidy and cellularity, and thus calculation of absolute copy number, were optimized through a combination of the **ACE**, **Rascal**, and **ichorCNA** bioinformatic tools. **Mixture modelling** was used to subgroup the six fundamental copy number features and **non-negative matrix factorization** was used to generate the signatures and cluster the samples.

Results

We extracted **six fundamental copy number features** from 69 diagnostic and pre-diagnostic cervical samples from patients diagnosed with HGSC and generated **six CN signatures**. We found different distributions of features in benign samples compared to tumors and cervical samples from HGSC patients. We also observed different exposures to the six signatures in different patient groups.

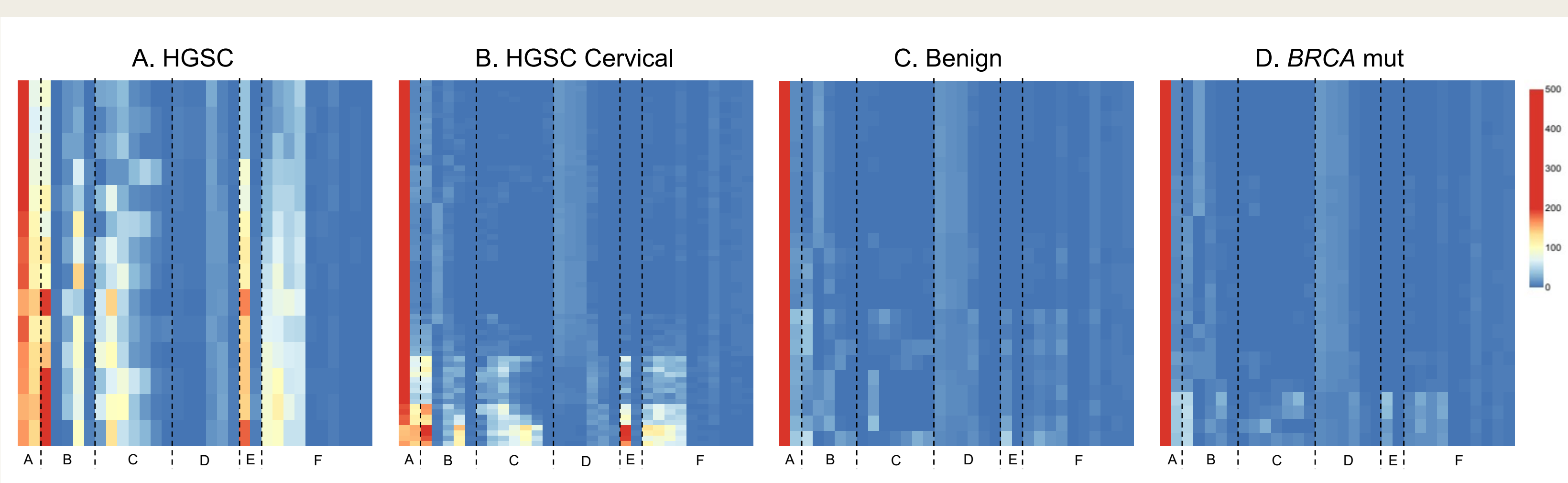


Figure 1. Sample-by-component matrix in different sample sets. X axis: 32 components grouped by the six fundamental features (A-F). A= breakpoints per 10Mb, B= copy number, C= CN change point, D= breakpoints per chromosome arm, E= length of segments with oscillating copy number and F= segment size.

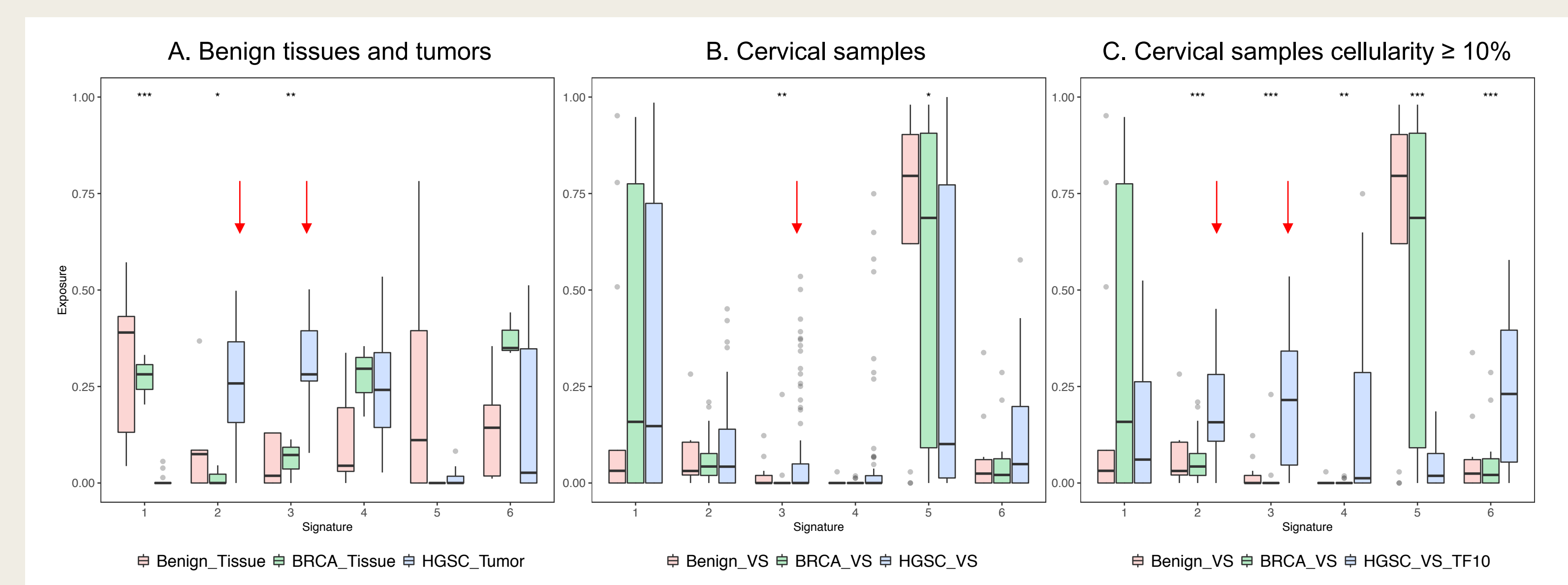


Figure 2. Signatures exposures in different sample sets. **A.** Tissue from controls (n=11), *BRCA* mutation carriers (n=7) and tumors (n=14). **B.** Cervical samples (CS) from controls (n=13), *BRCA* mutation carriers (n=20) and HGSC patients (n=69). **C.** CS from controls, *BRCA* mutation carriers and HGSC patients with cellularity $\geq 10\%$ (n=17).

Red arrows point out higher exposure to Signature 2 and 3 in tumors and cervical samples from HGSC patients. Significant differences are highlighted using asterisks (* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$).

Table 1. Patient and sample inclusion.

	Cohort 1 2015-16			Cohort 2 2018-20
	HGSC	<i>BRCA</i> mut	Benign	HGSC
FF tissue	X	X	X	X
Blood	X	X	X	X
Endometrial biopsy	X	X	X	X
Plasma	X	X	X	X
Liquid-based DNAgard®	X	X	X	
ThinPrep® slide	X	X	X	
Liquid-based ThinPrep®				X

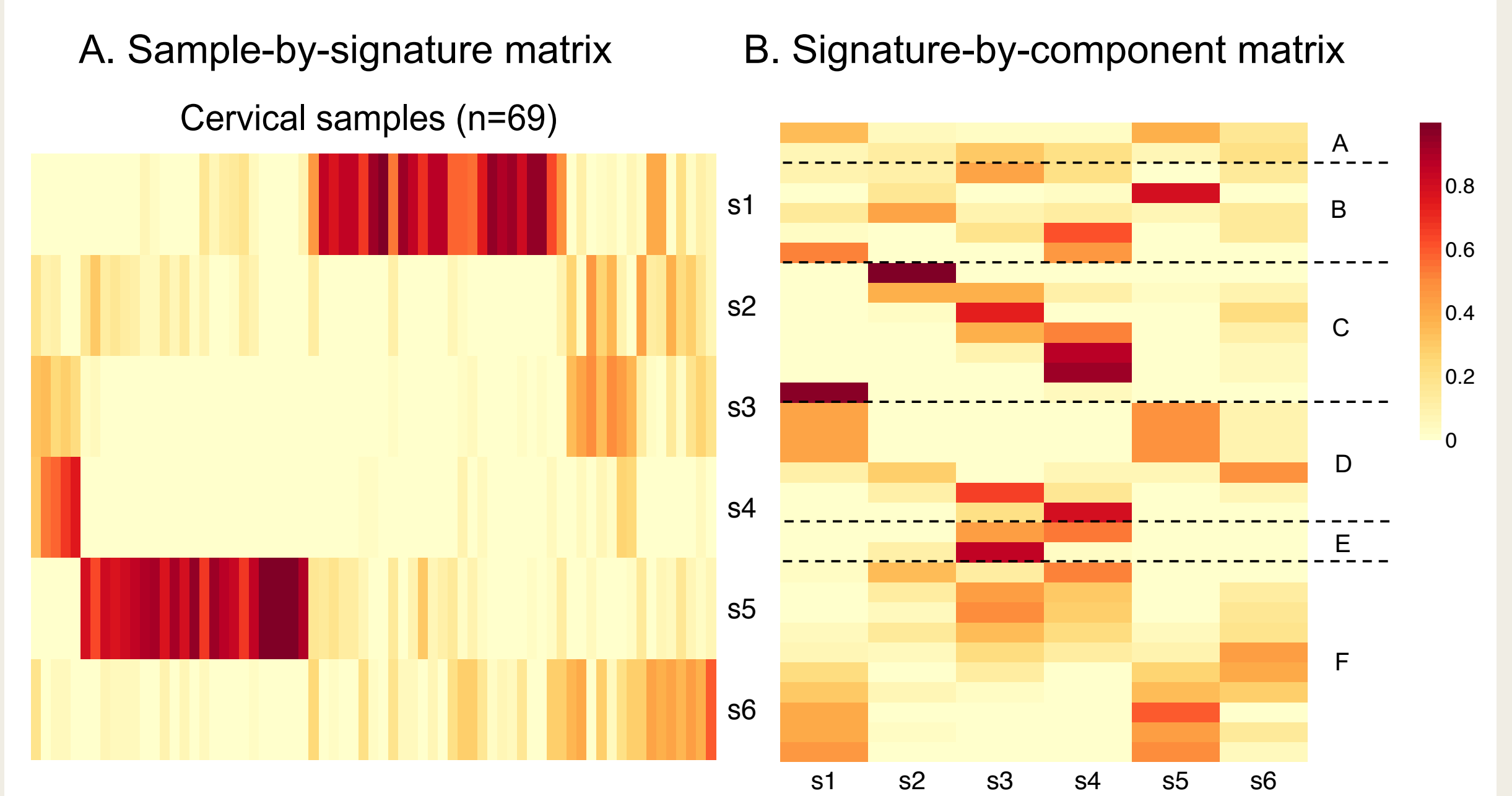


Figure 3. Construction of copy number signatures with cervical samples from HGSC patients (CerCNsig). **A.** Sample-by-signature matrix. **B.** Signature-by-component matrix.

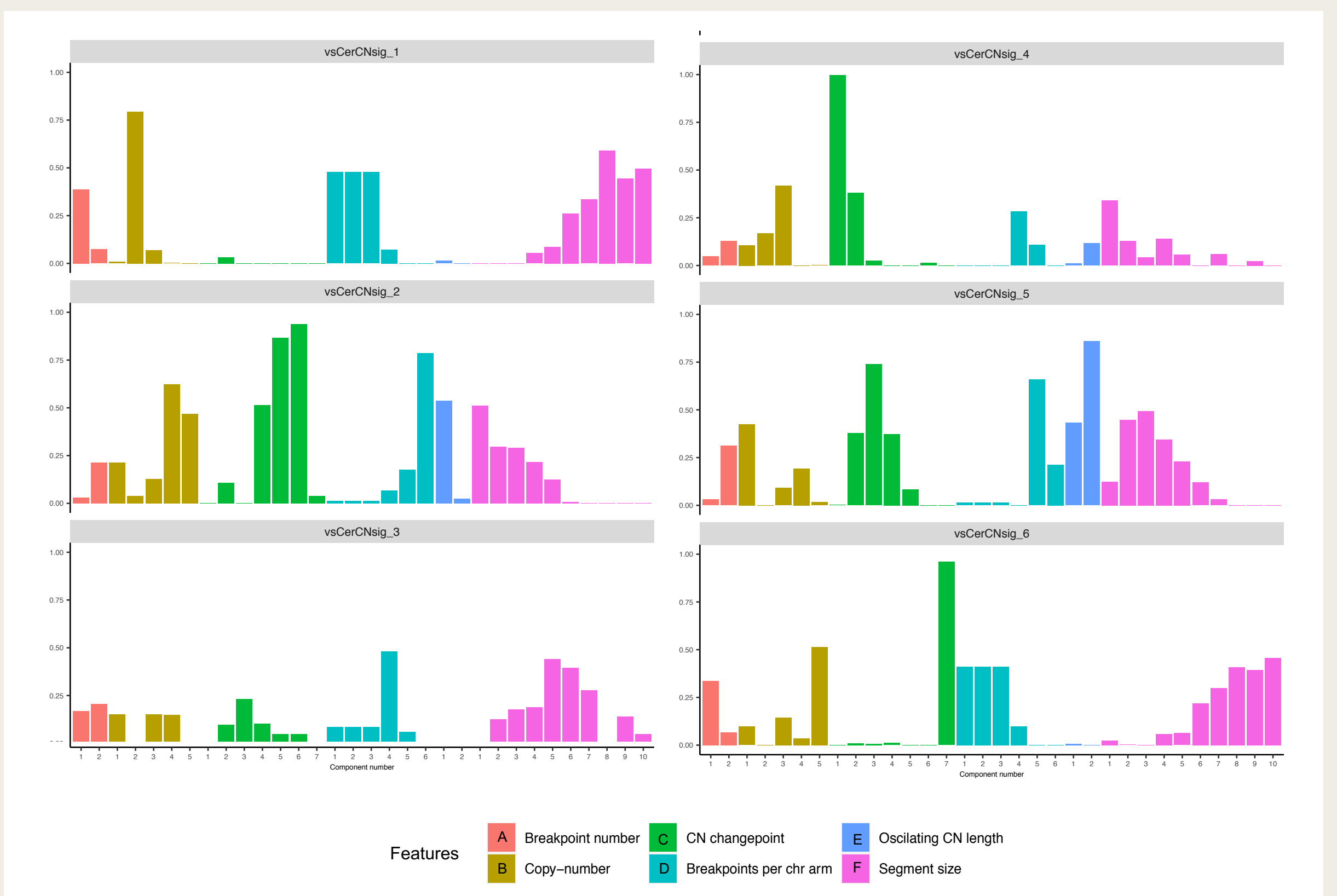


Figure 4. Distribution of features in the six copy number signatures, CerCNsig, in cervical samples from HGSC patients.

Conclusions

Further understanding of the components and cell types contributing to each signature, and inclusion of more cervical samples into the approach, will hopefully identify a novel tumorigenic signature for early detection of HGSC in cervical samples.

Contact

Laura Martin de la Fuente

Division of Oncology, Department of Clinical Sciences, Lund, Sweden

Lund University Cancer Center, Medicon Village 404-B3

SE-22381 Lund, Sweden

Email: laura.martin_de_la_fuente@med.lu.se