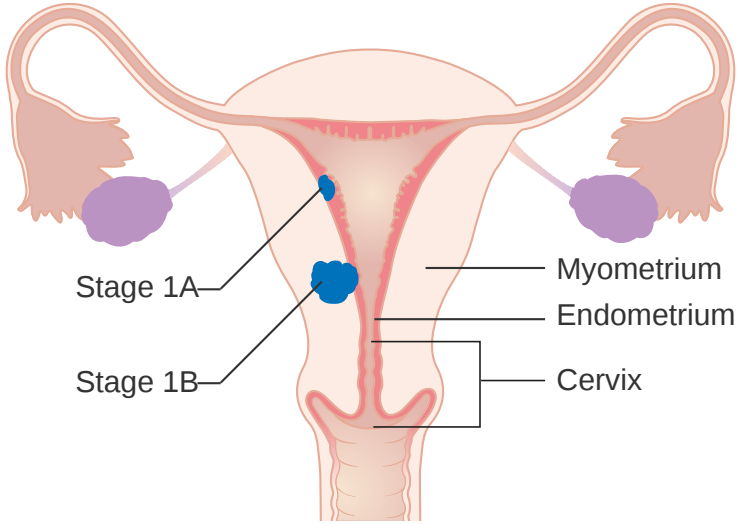
Classification of Endometrial cancer using Machine Learning

Robert Różański

Endometrial cancer



Type I (less aggressive):
- Endometroid adenocarcinoma

Type II (more aggressive):
- Serous cystadenocarcinoma
- Papillary serous adenocarcinoma
- Clear cell adenocarcinoma

https://en.wikipedia.org/wiki/Endometrial_cancer#/media/File:Diagram_showing_stage_1A_and_1B_cancer_of_the_womb_CRUK_196.svg

Data

QIAseq Targeted DNA Panels

Print

Digital DNA sequencing to confidently detect low-frequency variants

- **Digital sequencing enabled by molecular barcodes to remove PCR duplicates**
- **Complete Sample to Insight solution streamlines the workflow**
- **Compatibility with low-quality DNA enables efficient sequencing of FFPE and cfDNA samples**
- **Minimal DNA input to preserve precious samples**
- **Optimized buffers and conditions to achieve high coverage of GC-rich regions**

The QIAseq targeted DNA Panels have been developed as a complete Sample to Insight solution to enable digital DNA sequencing by utilizing molecular barcodes. Digital DNA sequencing is a unique approach to detect low-frequency variants with high confidence by overcoming the issues of PCR duplicates, false positives and library bias.

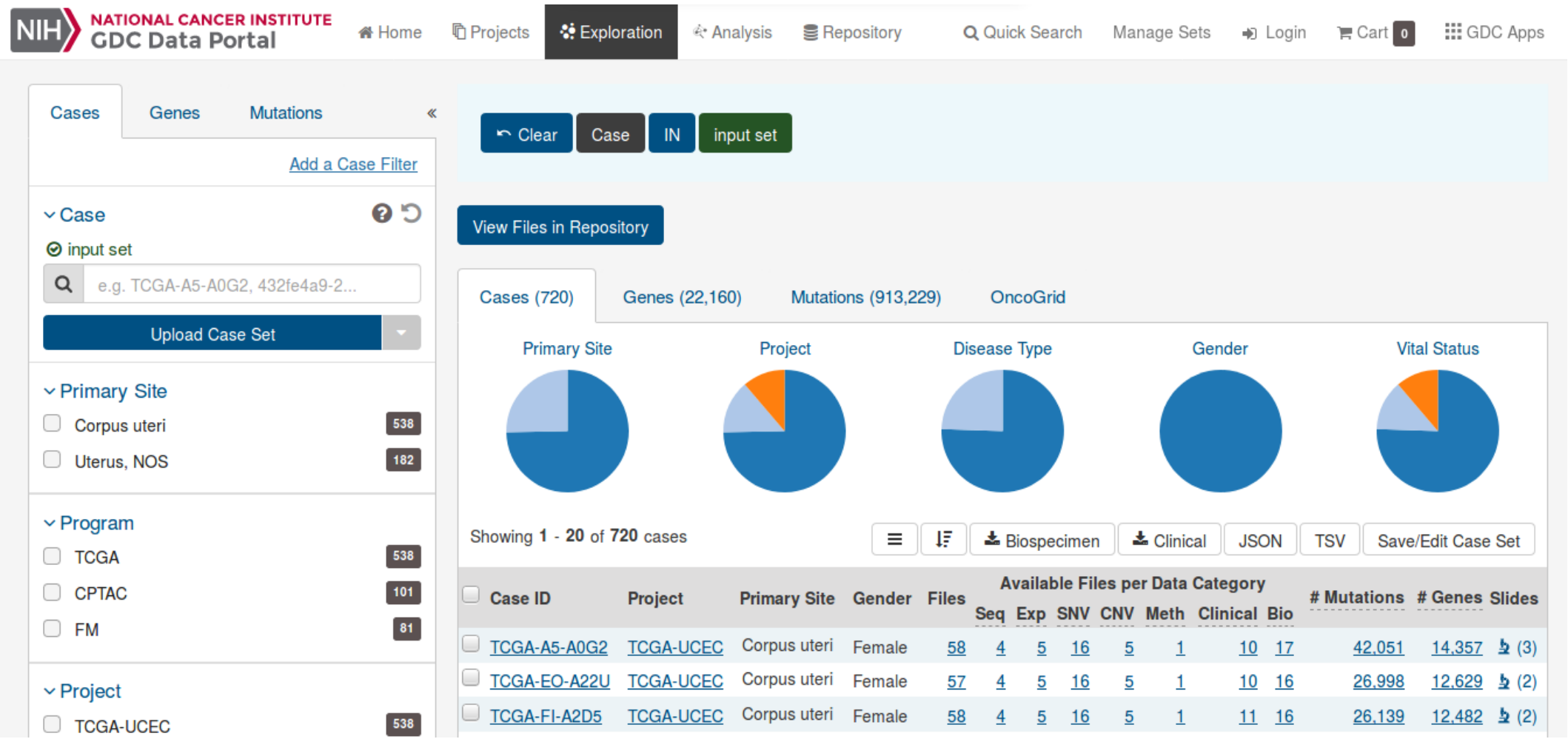
Data

Adenoma
Tubular Adenoma: BRAF, FBXW7, KRAS.
Tubulovillous Adenoma: BRAF, CTNNB1, KRAS, NRAS, PIK3CA (p110-alpha).
Villous Adenoma: BRAF, KRAS.
Other Adenoma-Related Genes: APC, DMD, SMAD4 (MADH4), STK11 (LKB1), TCF7L2.

Carcinoid-Endocrine Tumor
APC, CTNNB1, TP53 (p53).

Carcinoma
Adenocarcinoma: ACVR1B, AKT1, APC, ATM, ATP6V0D2, AXIN2, BAX, BLM, BMPR1A (ALK3), BRAF, BRCA1, BRCA2, BUB1B, CASP8 (FLICE), CDC27, CDH1 (E-Cadherin), CDK4, CDKN2A (p16INK4a), CHEK2 (RAD53), CTNNA1, CTNNB1, DCC, DMD, EGFR (ERBB1), ENG (EVI-1), EP300, EPCAM, ERBB2 (HER-2, NEU), FBXW7, FGFR3, FLCN, FZD3, GALNT12, GPC6, GREM1, KIT (CD117), KRAS, MAP2K4 (MKK4, JNKK1), MAP7, MET, MIER3, MLH1, MLH3, MSH2, MSH3, MSH6, MUTYH, MYO1B, NRAS, PALB2, PIK3CA (p110-alpha), PIK3R1 (p85-ALPHA), PMS1, PMS2, POLD1, POLE, PTEN, PTPN12, RET, RPS20, SLC9A9, SMAD2 (MADH2), SMAD4 (MADH4), SRC, STK11 (LKB1), TCERG1, TCF7L2, TGFBR2, TP53 (p53), WBSCR17.
Neuroendocrine: BRAF, KRAS.
Serrated Carcinoma: BRAF, PIK3CA (p110-alpha).
Squamous Cell Carcinoma: KRAS, TP53 (p53).
Other Carcinomas: BRCA2, CDKN2A (p16INK4a).

Training Data



https://portal.gdc.cancer.gov/exploration?filters=%7B%22content%22%3A%5B%7B%22content%22%3A%7B%22field%22%3A%22cases.case_id%22%2C%22value%22%3A%5B%22set_id%3AAWxYARM-1FJwHPndQLUN%22%5D%7D%2C%22op%22%3A%22IN%22%7D%5D%2C%22op%22%3A%22AND%22%7D

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Feature engineering: genes and VEPs

genes

case_id	type	diagnosis	ACVR1B	AKT1	ALK3	APC	ATM	ATP6V0D2
8a0a58a0-5	2	Serous cyst	0	0	0	0	0	0
4db38349-2	1	Endometrioi	1	0	0	1	1	0
119b1761-a	1	Endometrioi	0	1	0	1	1	1
435b57e7-5	1	Endometrioi	1	1	0	1	1	1

VEP 1

case_id	type	diagnosis	('ACVR1B', 'HIGH')	('ACVR1B', 'LOW')	('ACVR1B', 'MODERATE')	('ACVR1B', 'MODIFIER')	('AKT1', 'HIGH')	('AKT1', 'LOW')
8a0a58a0-5	2	Serous cyst	0	0	0	0	0	0
4db38349-2	1	Endometrioi	0	0	1	1	0	0
119b1761-a	1	Endometrioi	0	0	0	0	0	0
435b57e7-5	1	Endometrioi	0	0	0	1	0	0

VEP 2

case_id	type	diagnosis	('ACVR1B', 'MODIFIER')	('ACVR1B', 'VEP_SCORE'	('AKT1', 'MODIFIER')	('AKT1', 'VEP_SCORE')	('ALK3', 'MODIFIER')	('ALK3', 'VEP_SCORE')
8a0a58a0-5	2	Serous cyst	0	0	0	0	0	0
4db38349-2	1	Endometrioi	1	2	0	0	0	0
119b1761-a	1	Endometrioi	0	0	1	2	0	0
435b57e7-5	1	Endometrioi	1	0	1	2	0	0

VEP 3

case_id	type	diagnosis	ACVR1B	AKT1	ALK3	APC	ATM	ATP6V0D2
8a0a58a0-5	2	Serous cyst	0	0	0	0	0	0
4db38349-2	1	Endometrioi	2	0	0	3	3	0
119b1761-a	1	Endometrioi	0	2	0	2	3	3
435b57e7-5	1	Endometrioi	0	2	0	2	2	2

Feature engineering: genes and VEPs

Genes: 0.867

case_id	type	diagnosis	ACVR1B	AKT1	ALK3	APC	ATM	ATP6V0D2
8a0a58a0-5	2	Serous cyst	0	0	0	0	0	0
4db38349-2	1	Endometrioi	1	0	0	1	1	0
119b1761-a	1	Endometrioi	0	1	0	1	1	1
435b57e7-5	1	Endometrioi	1	1	0	1	1	1

VEP 1: 0.882

case_id	type	diagnosis	('ACVR1B', 'HIGH')	('ACVR1B', 'LOW')	('ACVR1B', 'MODERATE')	('ACVR1B', 'MODIFIER')	('AKT1', 'HIGH')	('AKT1', 'LOW')
8a0a58a0-5	2	Serous cyst	0	0	0	0	0	0
4db38349-2	1	Endometrioi	0	0	1	1	0	0
119b1761-a	1	Endometrioi	0	0	0	0	0	0
435b57e7-5	1	Endometrioi	0	0	0	1	0	0

VEP 2: 0.881

case_id	type	diagnosis	('ACVR1B', 'MODIFIER')	('ACVR1B', 'VEP_SCORE')	('AKT1', 'MODIFIER')	('AKT1', 'VEP_SCORE')	('ALK3', 'MODIFIER')	('ALK3', 'VEP_SCORE')
8a0a58a0-5	2	Serous cyst	0	0	0	0	0	0
4db38349-2	1	Endometrioi	1	2	0	0	0	0
119b1761-a	1	Endometrioi	0	0	1	2	0	0
435b57e7-5	1	Endometrioi	1	0	1	2	0	0

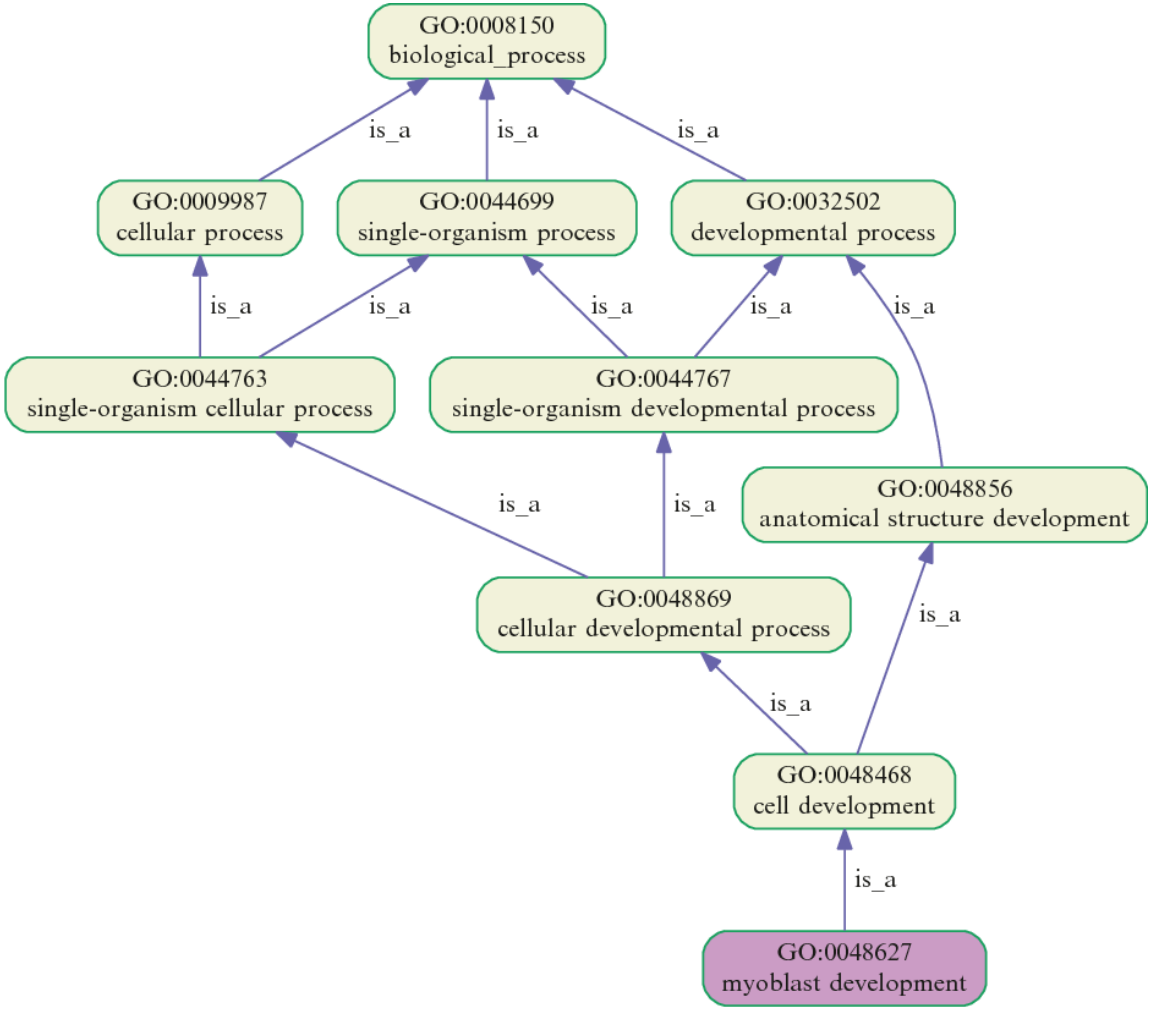
VEP 3: 0.885

case_id	type	diagnosis	ACVR1B	AKT1	ALK3	APC	ATM	ATP6V0D2
8a0a58a0-5	2	Serous cyst	0	0	0	0	0	0
4db38349-2	1	Endometrioi	2	0	0	3	3	0
119b1761-a	1	Endometrioi	0	2	0	2	3	3
435b57e7-5	1	Endometrioi	0	2	0	2	2	2

Feature engineering: Gene Ontology

case_id	GO:	GO:0006355	GO:0006468	GO:0006508	GO:0006511	GO:0006886	GO:0006915	GO:0006954
8a0a58a0-5	0	2	4	0	0	0	0	0
4db38349-2	0	10	16	3	0	0	14	0
119b1761-a	0	4	14	2	0	0	11	2
435b57e7-5	0	6	17	3	3	0	20	4

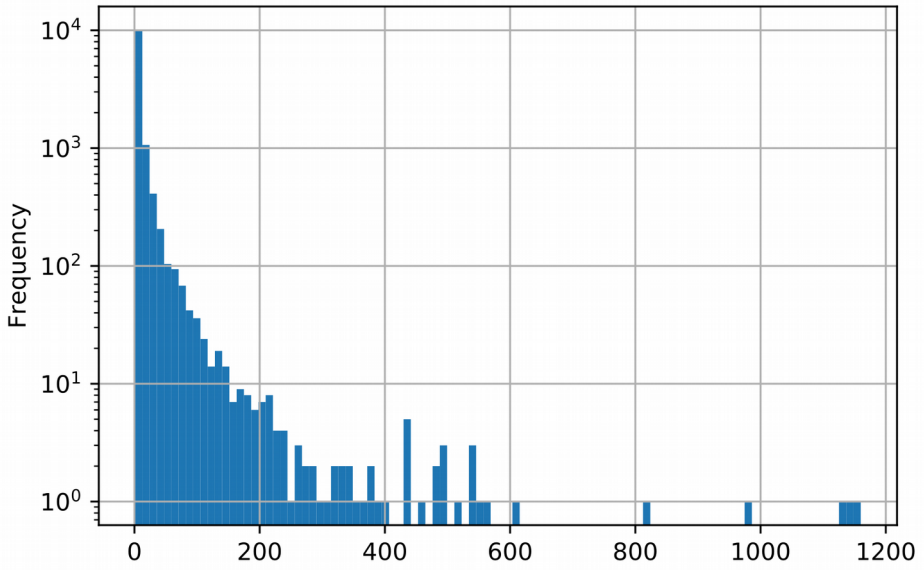
Feature engineering: Gene Ontology



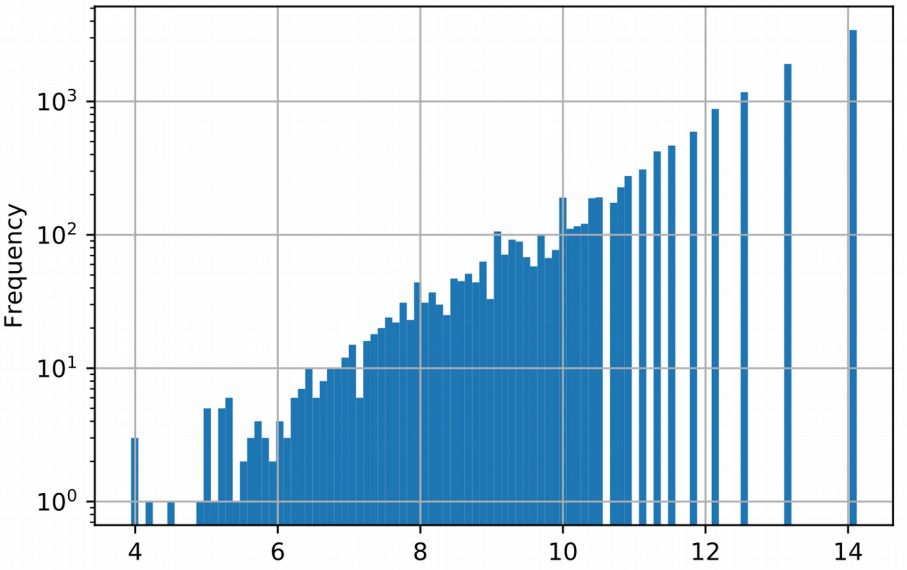
https://www.semanticscholar.org/paper/A-Gene-Ontology-Tutorial-in-Python.-Vesztrocy-Dessimoz/fa5a595b9bdb06b821206aa5664902686c3aadb5

Feature engineering: Gene Ontology

nb. of genes / GO term



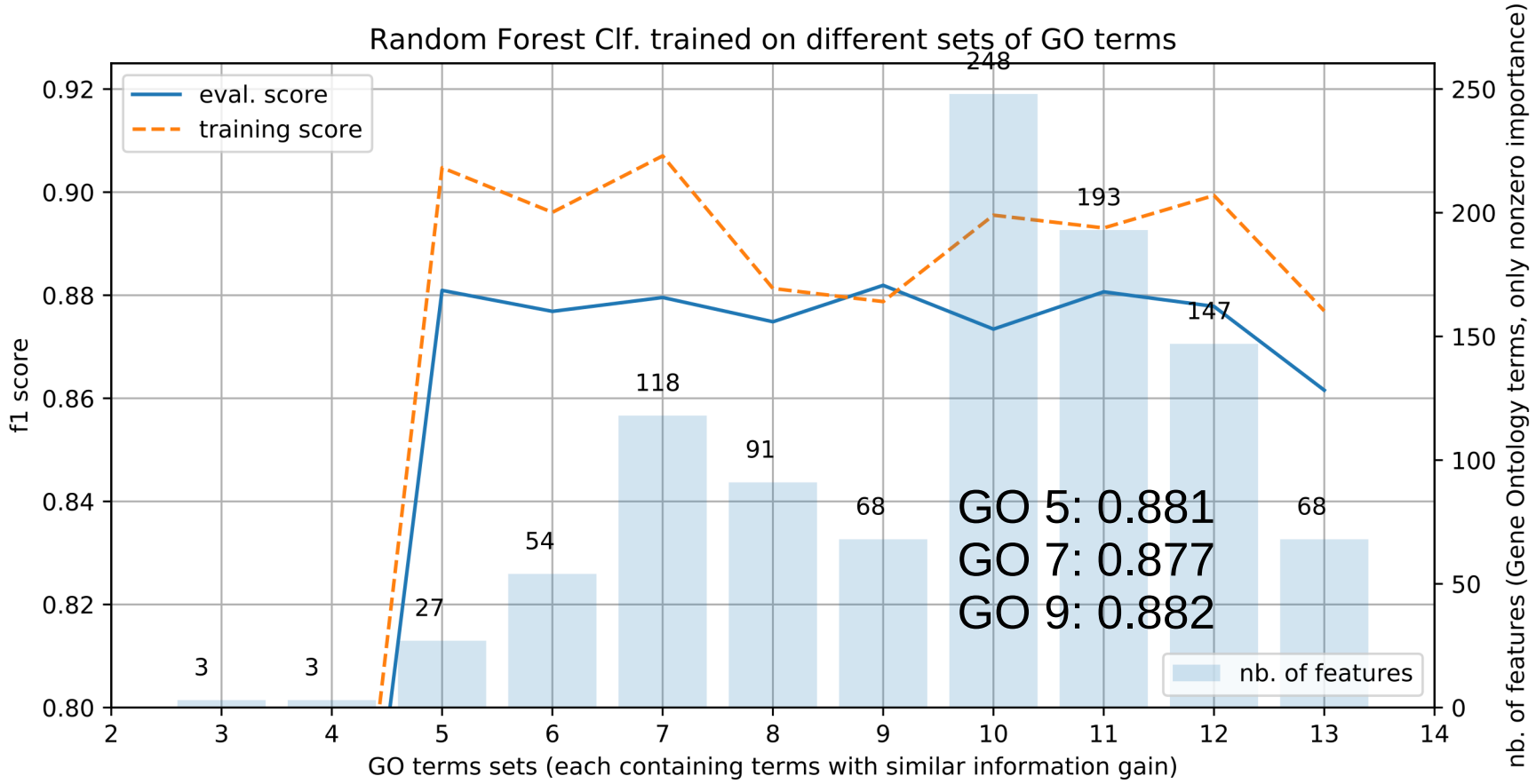
information gain



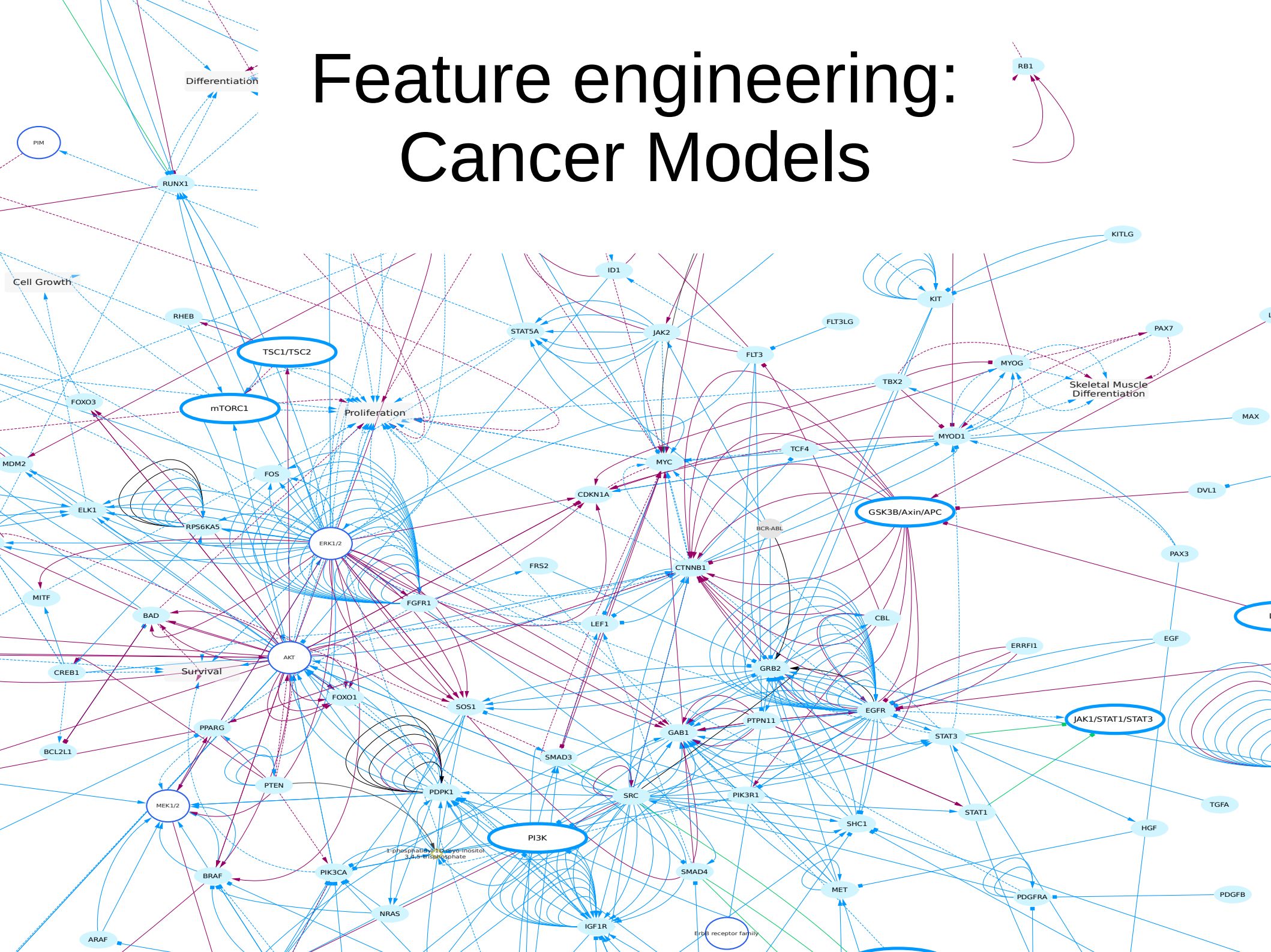
Alterovitz et al., “GO PaD: The Gene Ontology partition database”

Feature engineering: Gene Ontology

case_id	GO:	GO:0006355	GO:0006468	GO:0006508	GO:0006511	GO:0006886	GO:0006915	GO:0006954
8a0a58a0-5	0	2	4	0	0	0	0	0
4db38349-2	0	10	16	3	0	0	14	0
119b1761-a	0	4	14	2	0	0	11	2
435b57e7-5	0	6	17	3	3	0	20	4



Feature engineering: Cancer Models



Feature engineering: Cancer Models

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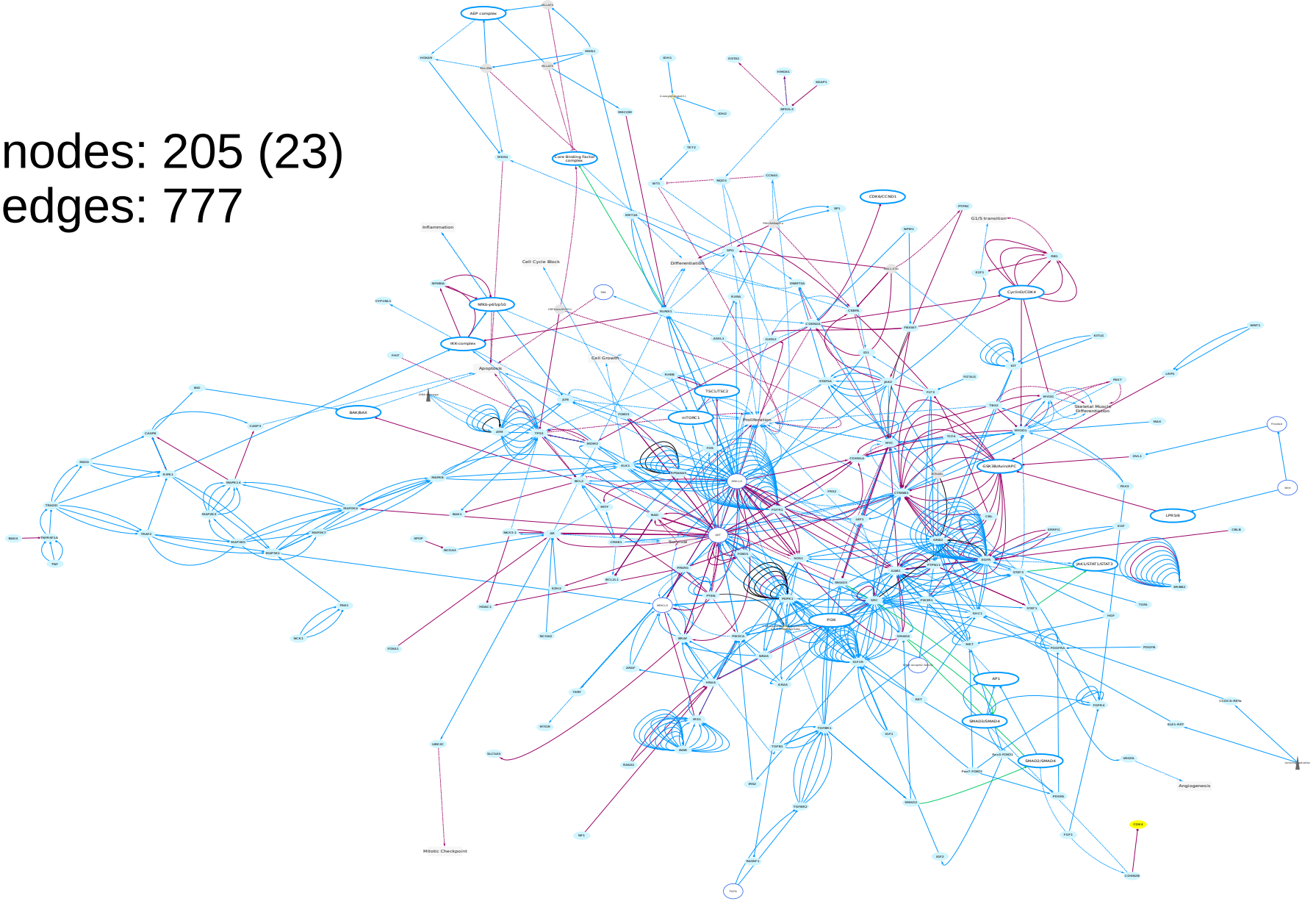
edges: 777



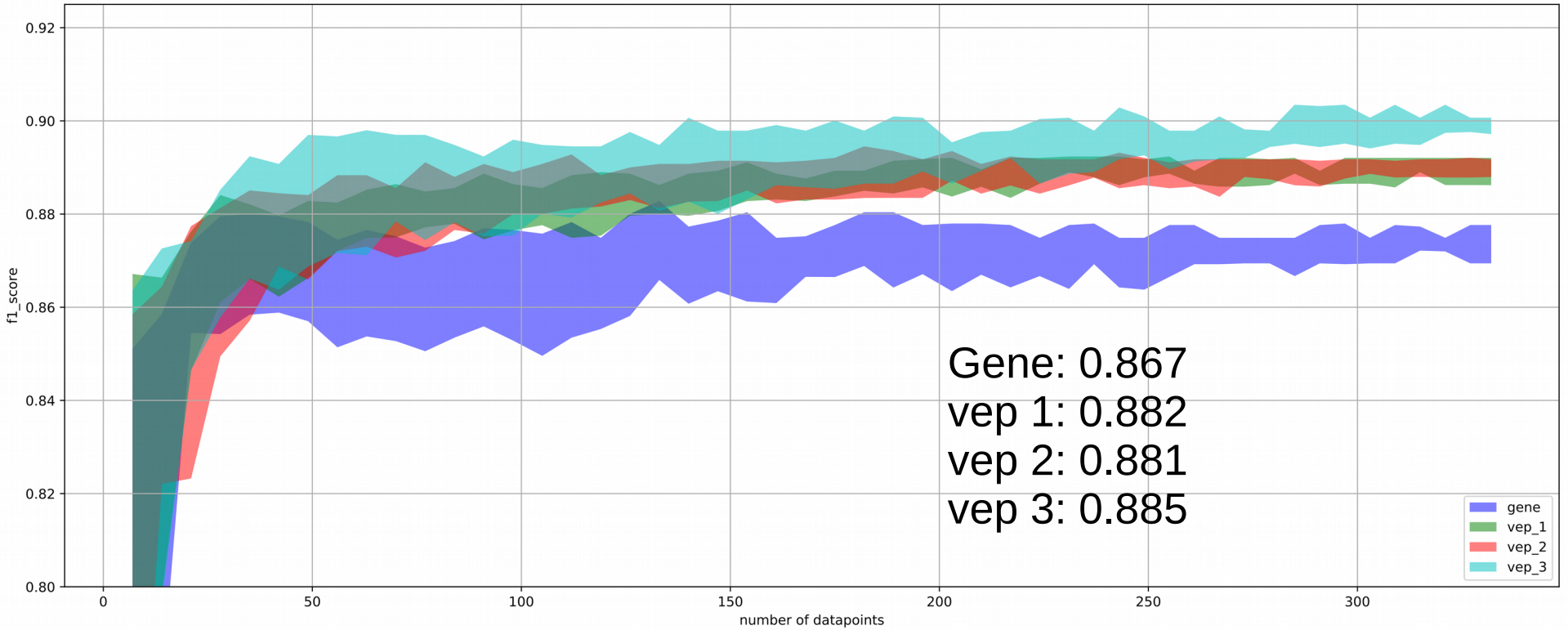
Feature engineering: Cancer Models

case_id	type	diagnosis	Core Binding Factor comp	1-phosphatidyl-1D-myo-ino	2-oxoglutarate(2-)	AEP complex	AKT	AP1
8a0a58a0-5	2	Serous cyst	0	2	0	0	2	0
4db38349-2	1	Endometrioi	0	5	0	0	4	0
119b1761-a	1	Endometrioi	0	7	0	0	5	0
435b57e7-5	1	Endometrioi	0	5	0	0	5	0

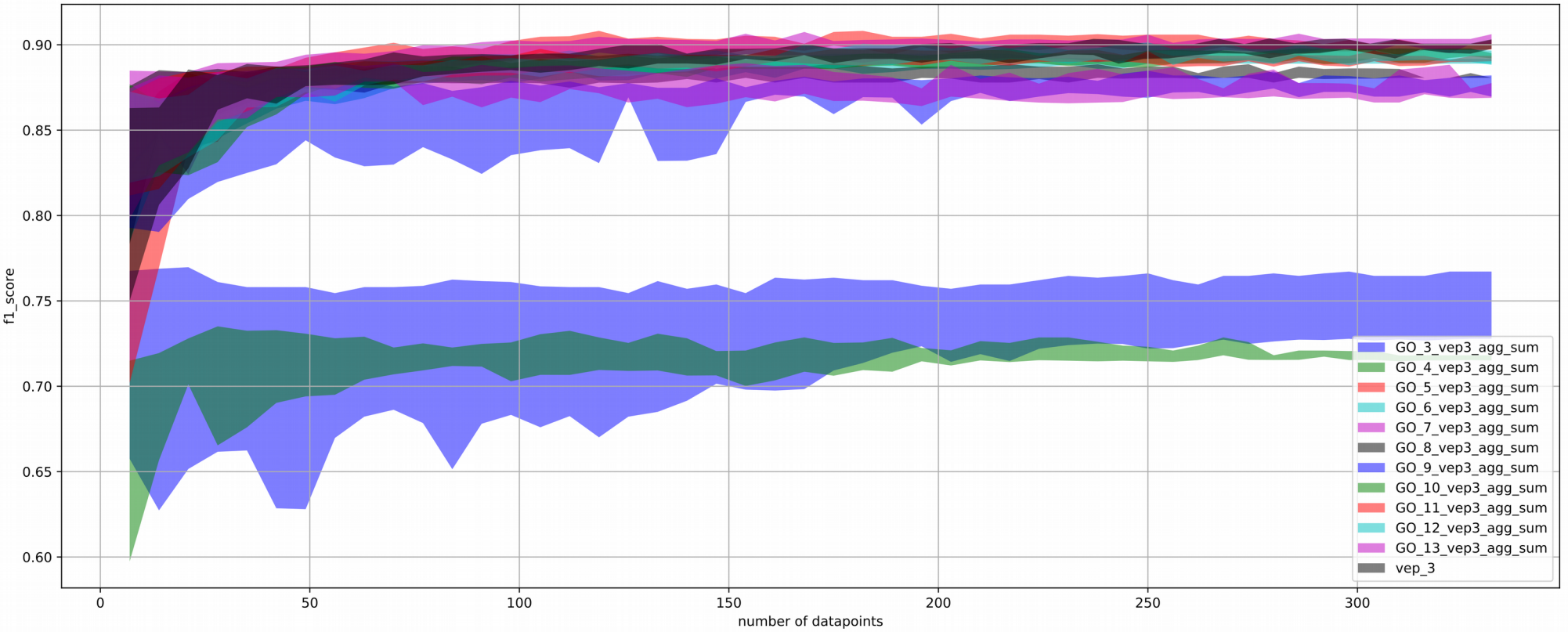
Summary

Gene	VEP 3	GO 5	GO 7	GO 9	model
0.867	0.885	0.881	0.877	0.882	0.896
89*	89*	33	209	68	168

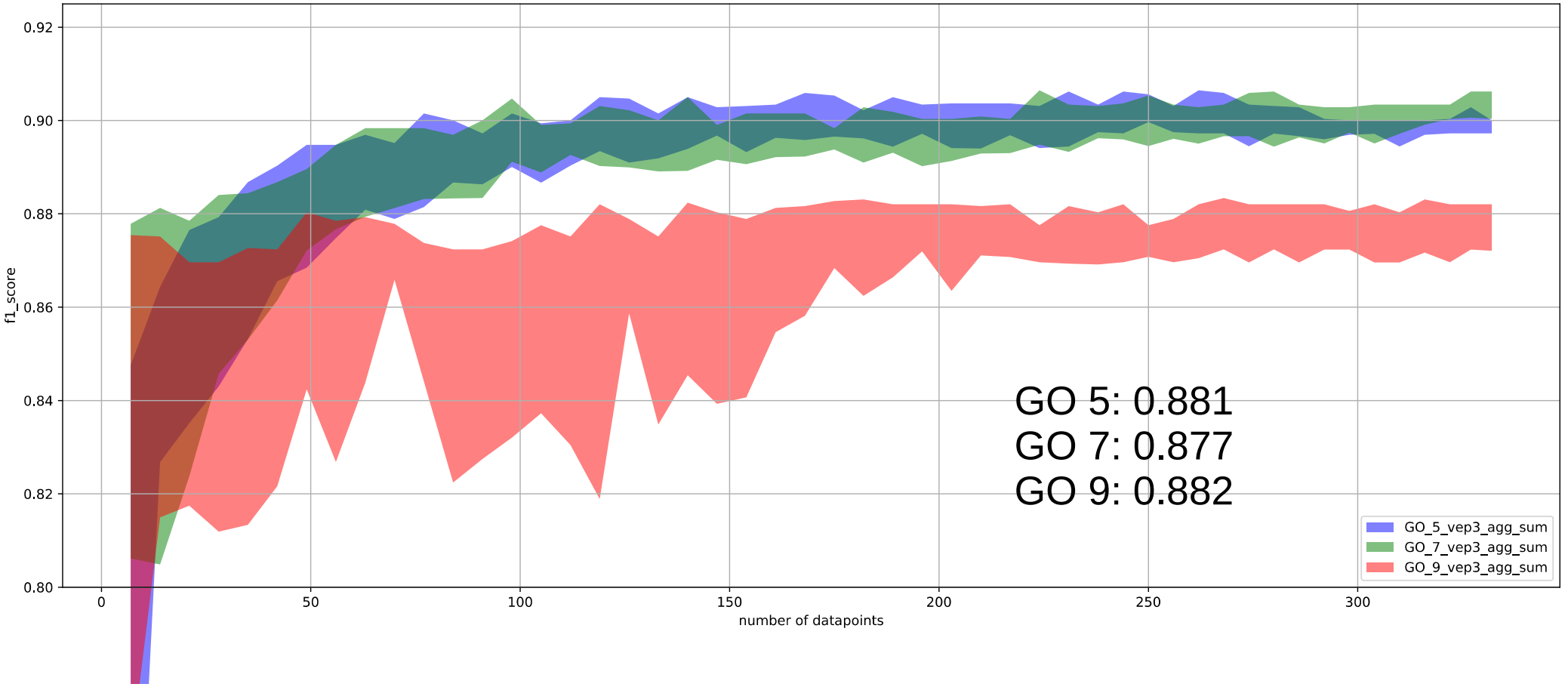
Feature engineering: genes and VEPs



Feature engineering: Gene Ontology

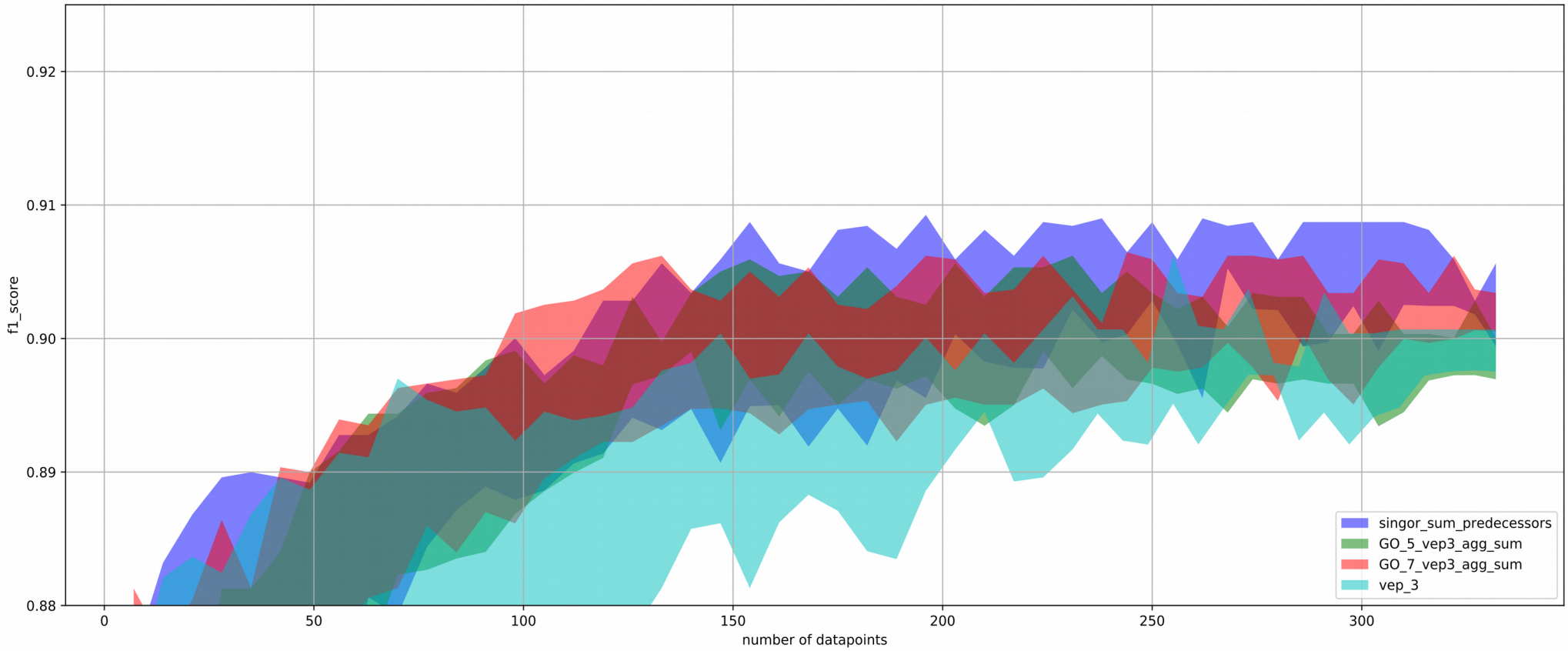
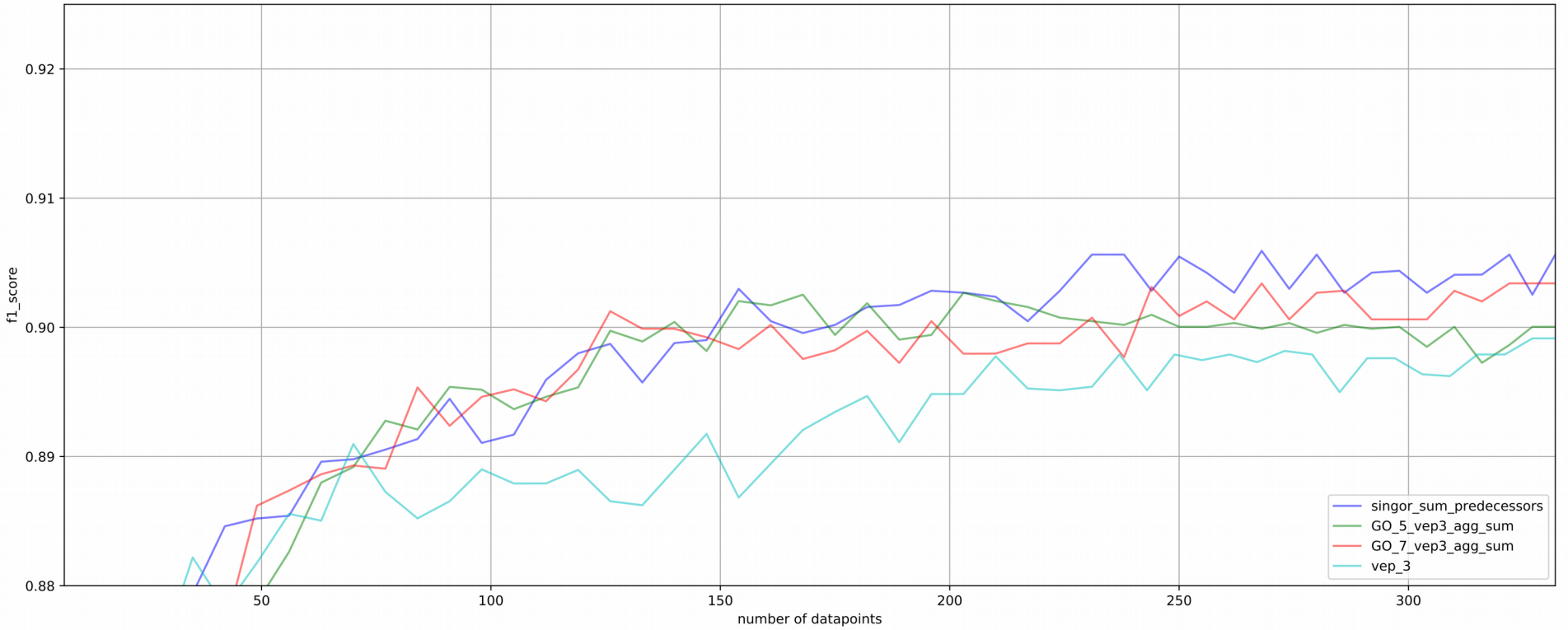


Feature engineering: Gene Ontology



Feature engineering: Cancer Models

case_id	type	diagnosis	Core Binding Factor comp	1-phosphatidyl-1D-myo-ino	2-oxoglutarate(2-)	AEP complex	AKT	AP1
8a0a58a0-5	2	Serous cyst	0	2	0	0	2	0
4db38349-2	1	Endometrioi	0	5	0	0	4	0
119b1761-a	1	Endometrioi	0	7	0	0	5	0
435b57e7-5	1	Endometrioi	0	5	0	0	5	0



Feature engineering: Cancer Models