Genomic Expression Analysis of Squamous Cell Lung Cancer

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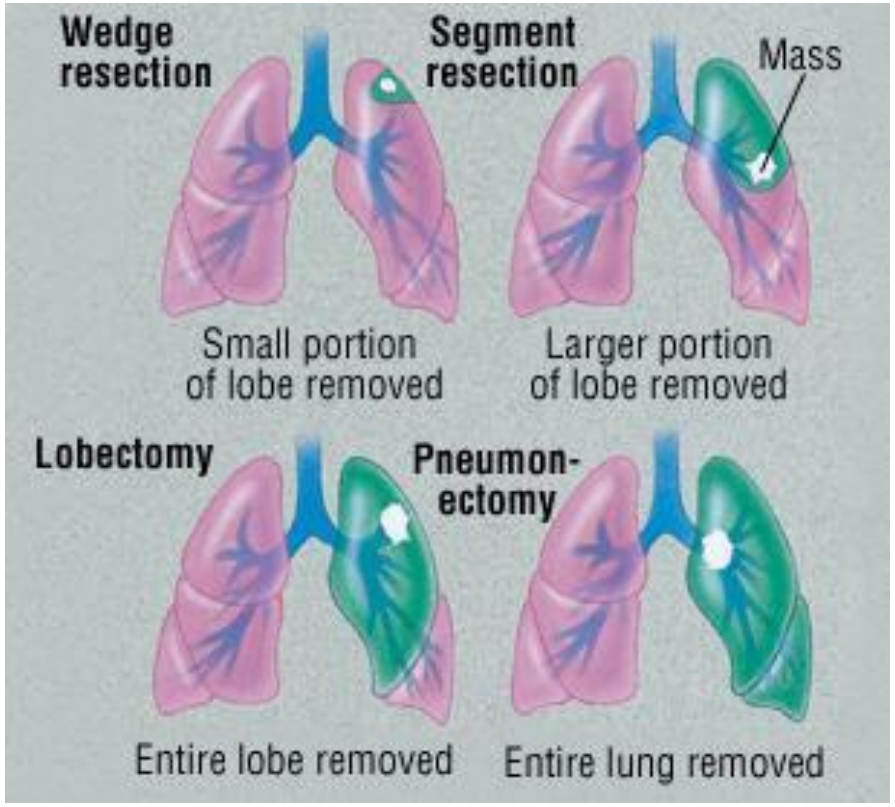
Squamous Cell Lung Cancer

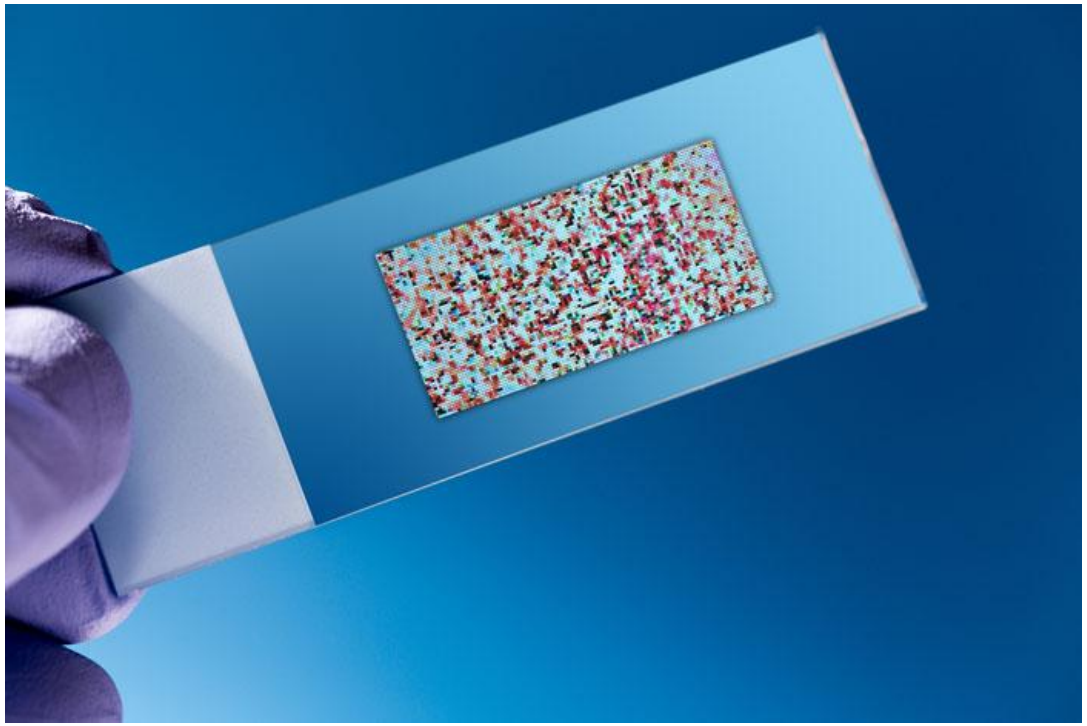
- Approx: 230k cases lung cancer per year –51% Men 49% Women
- Average age diagnosis 70
- 135k deaths per year

- 30% or Approx. 69k cases squamous cell lung cancer
- Starts in center of lung – treated by removing tumor/section of lung
- Prognosis is poor, less than 16% of patients survive 5 years or longer

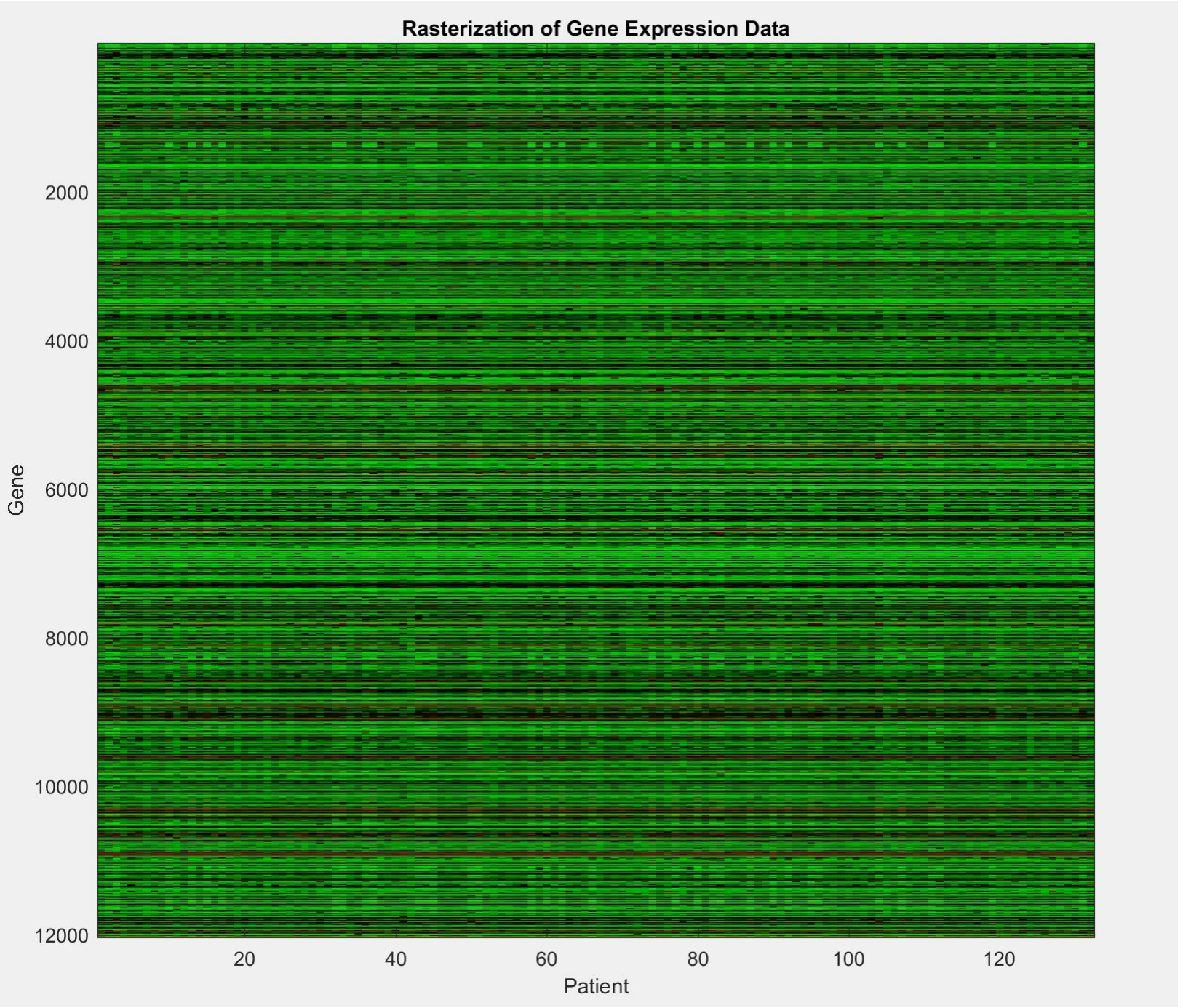


Data – Microarray Gene Expression

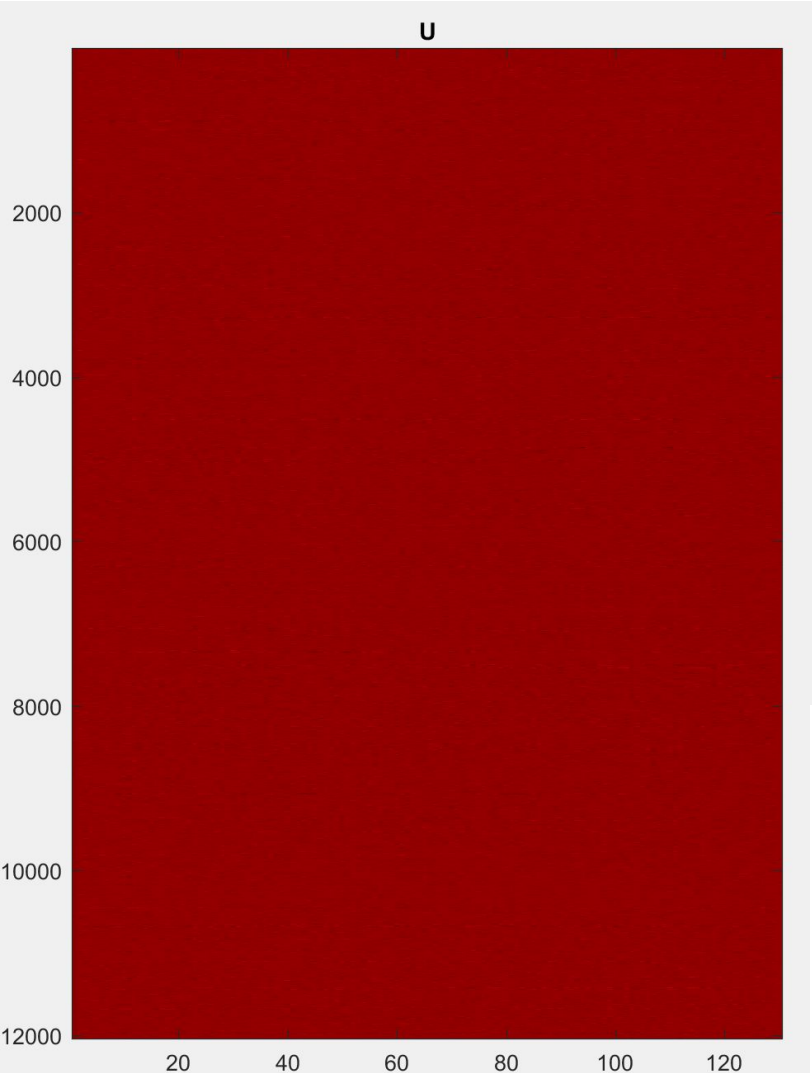
- Affymetrix Human Genome U133 Array
- 132 patients – 35 women & 97 men
- Average age at diagnosis = 66.2 years
- 5 Non-smokers
- 20 Current Smokers
- 107 Reformed Smokers

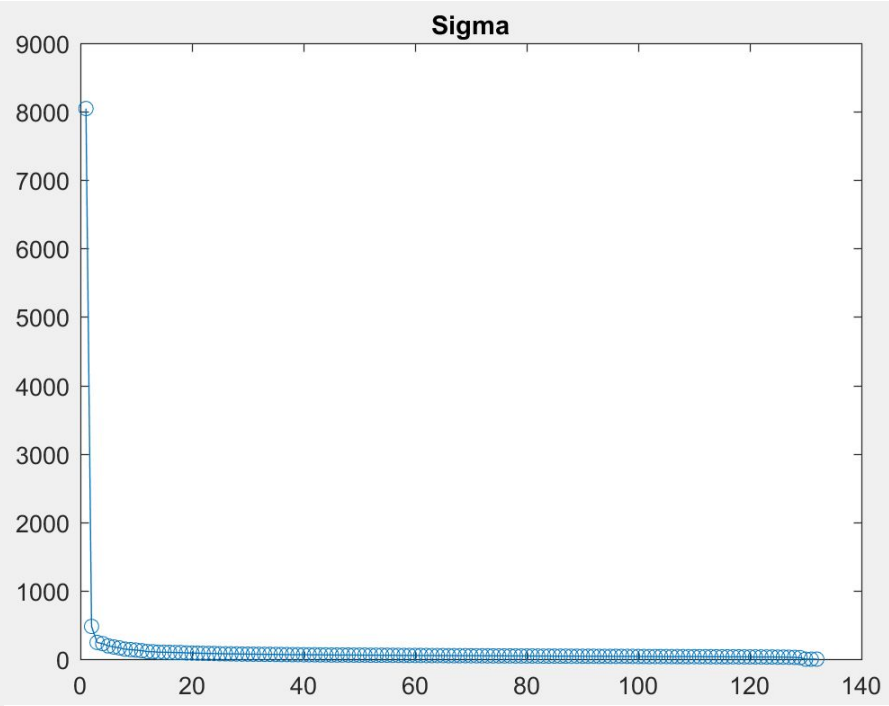


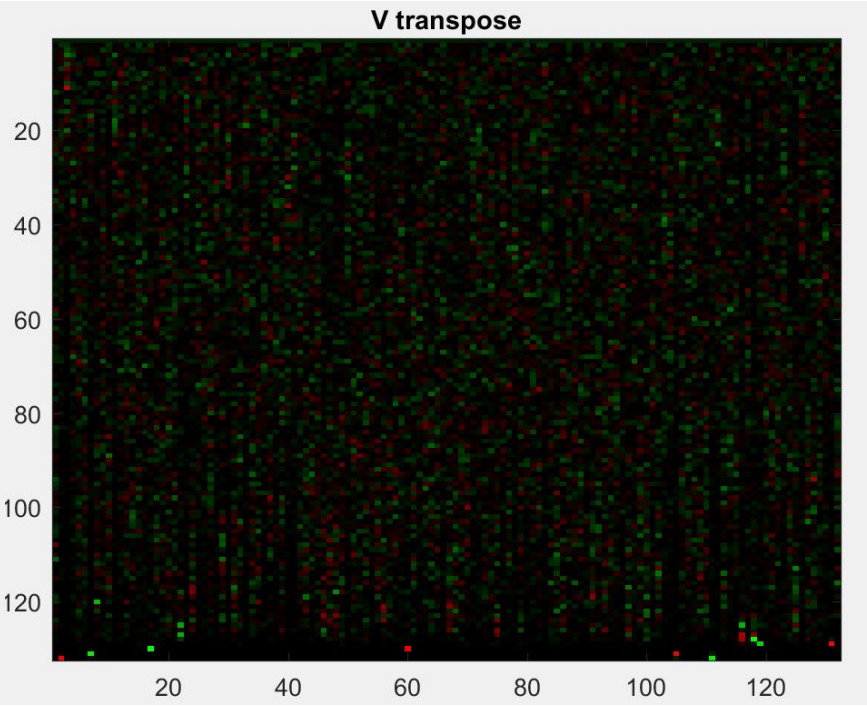
Rasterized Data



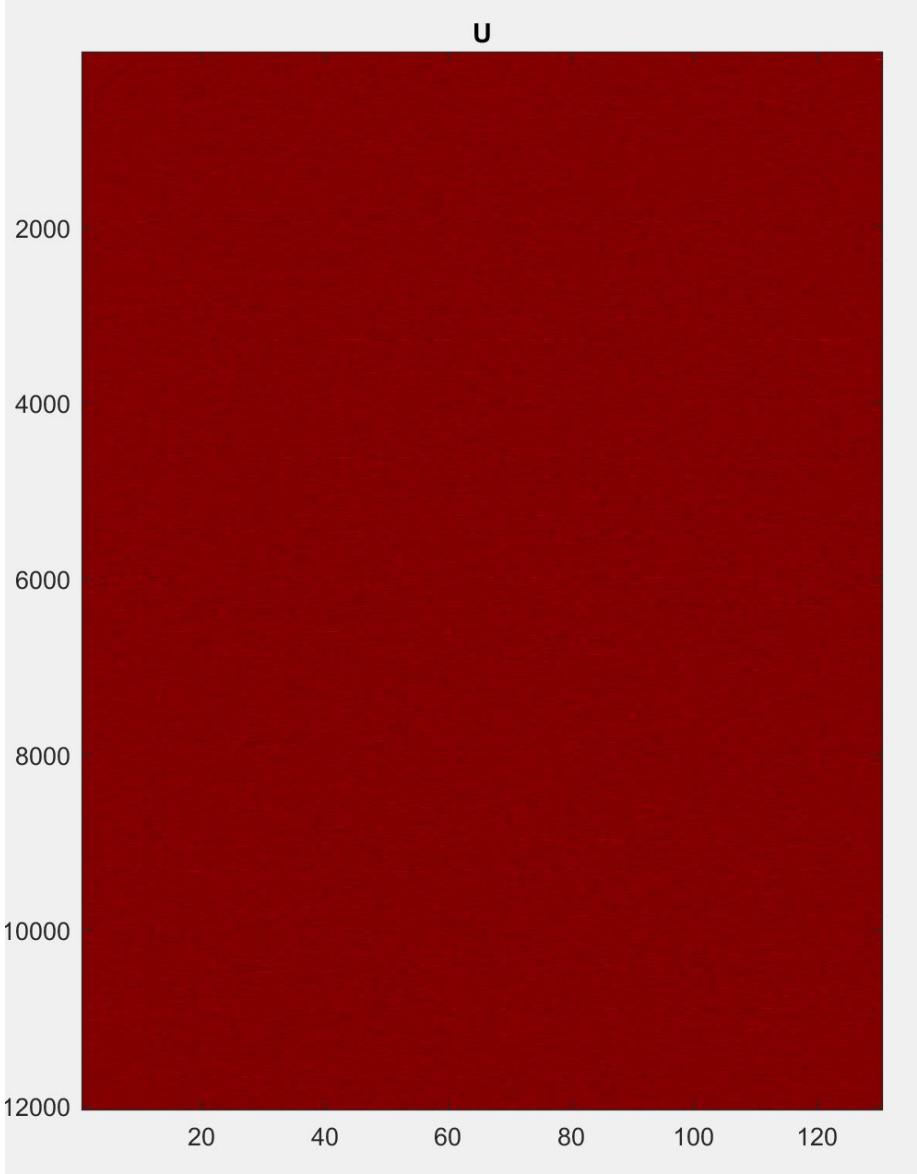
SVD of Unsorted Data

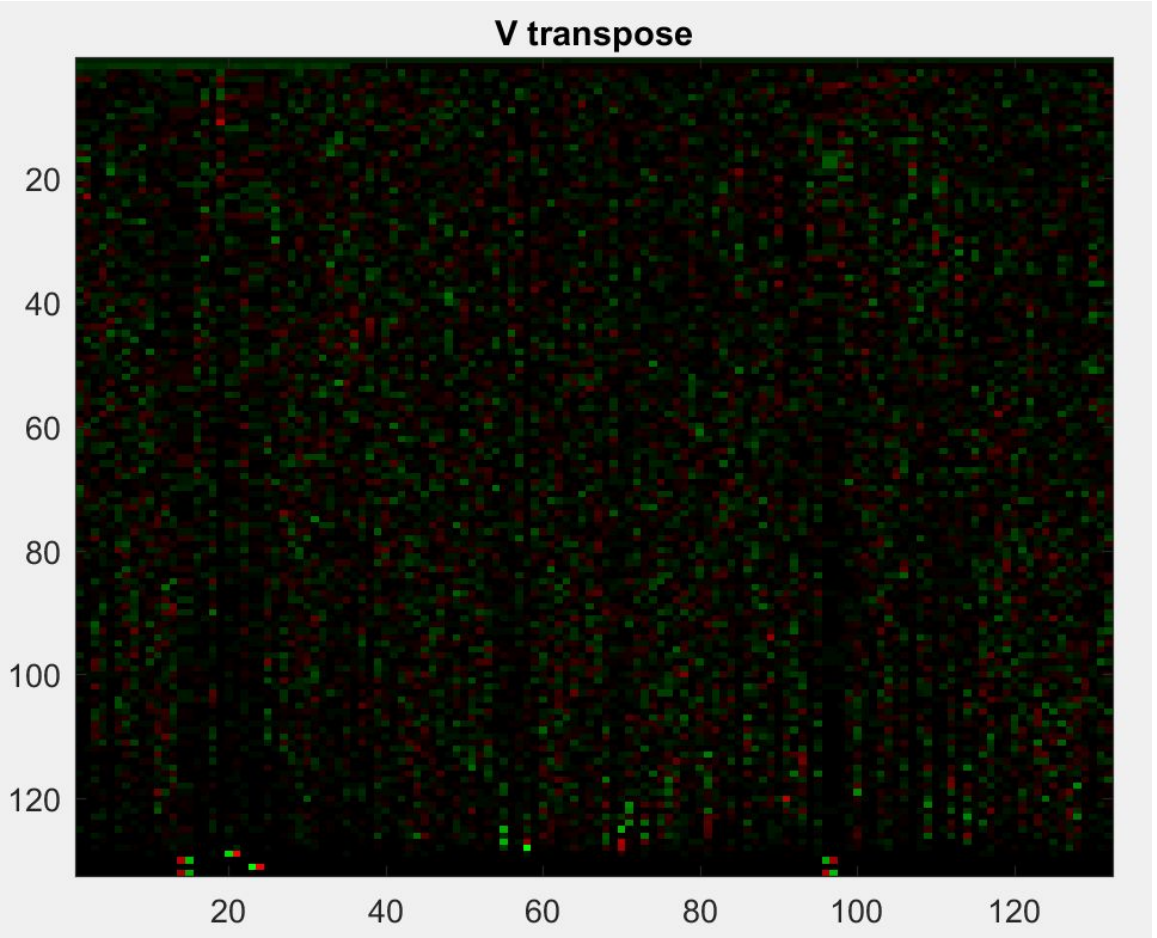




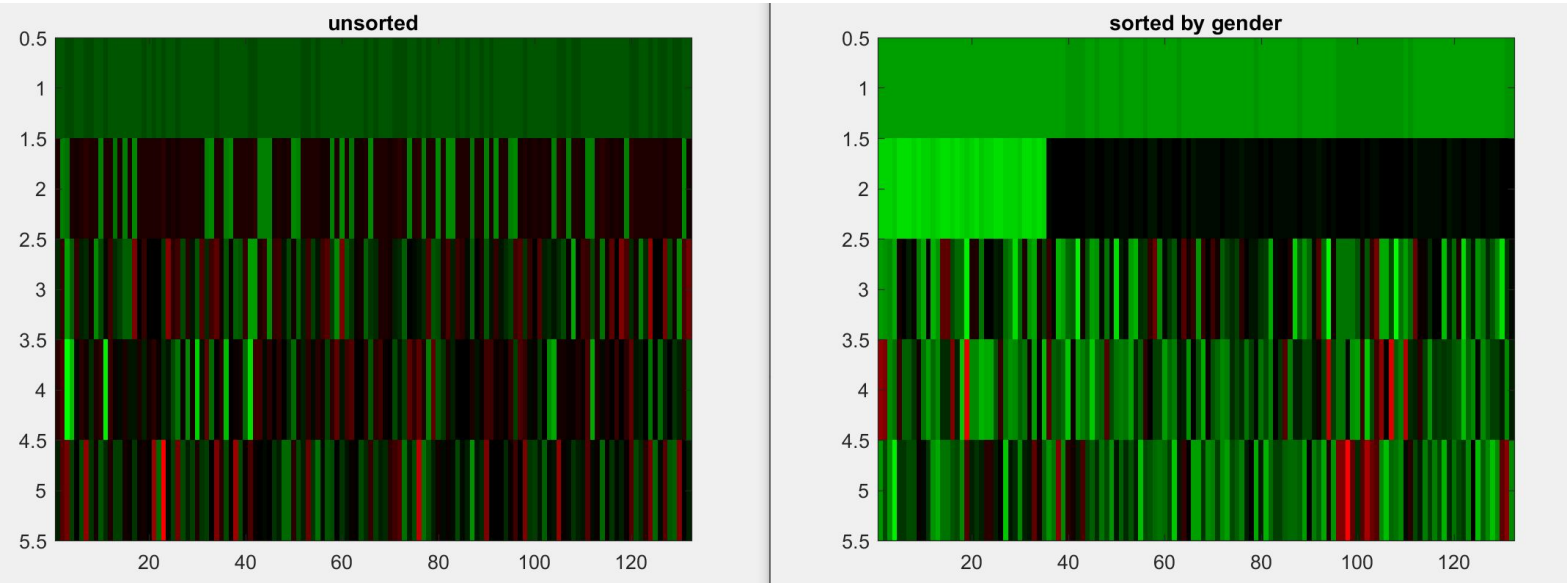


SVD of Data Sorted by Gender



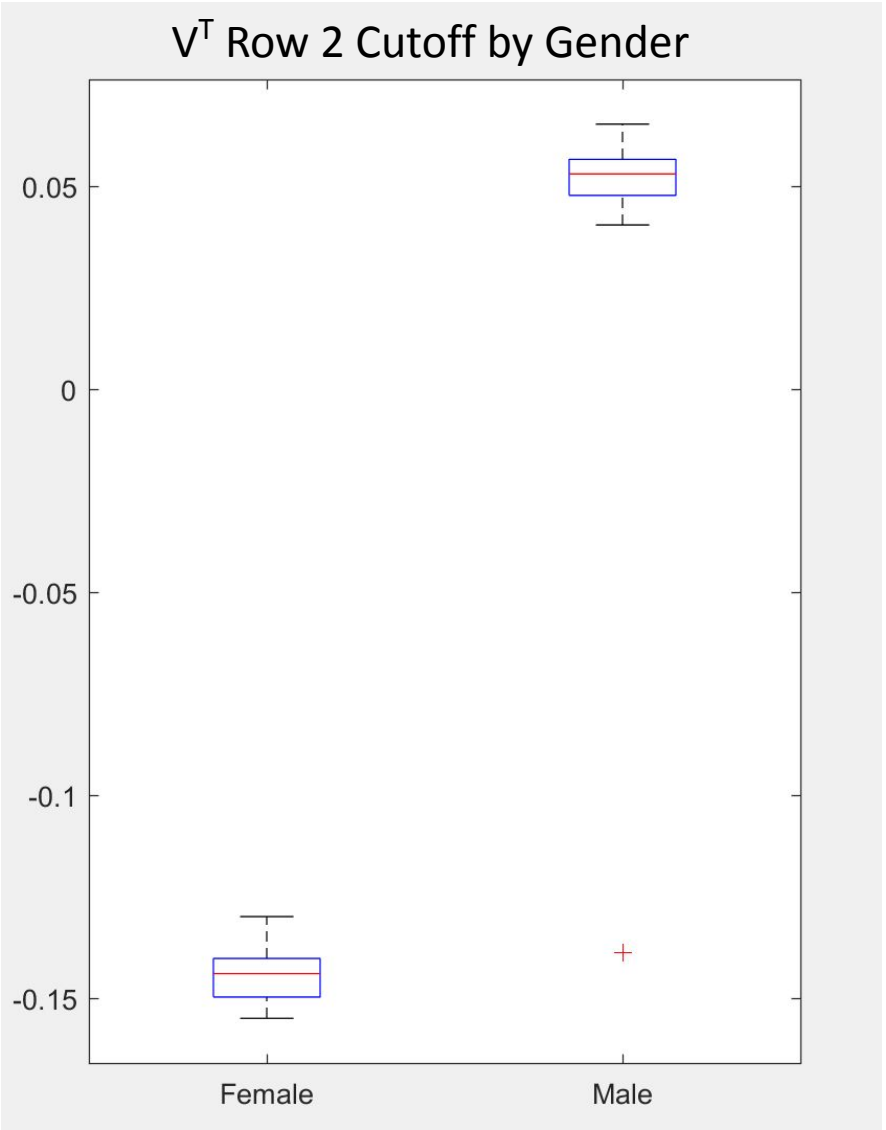


Comparison of V^T



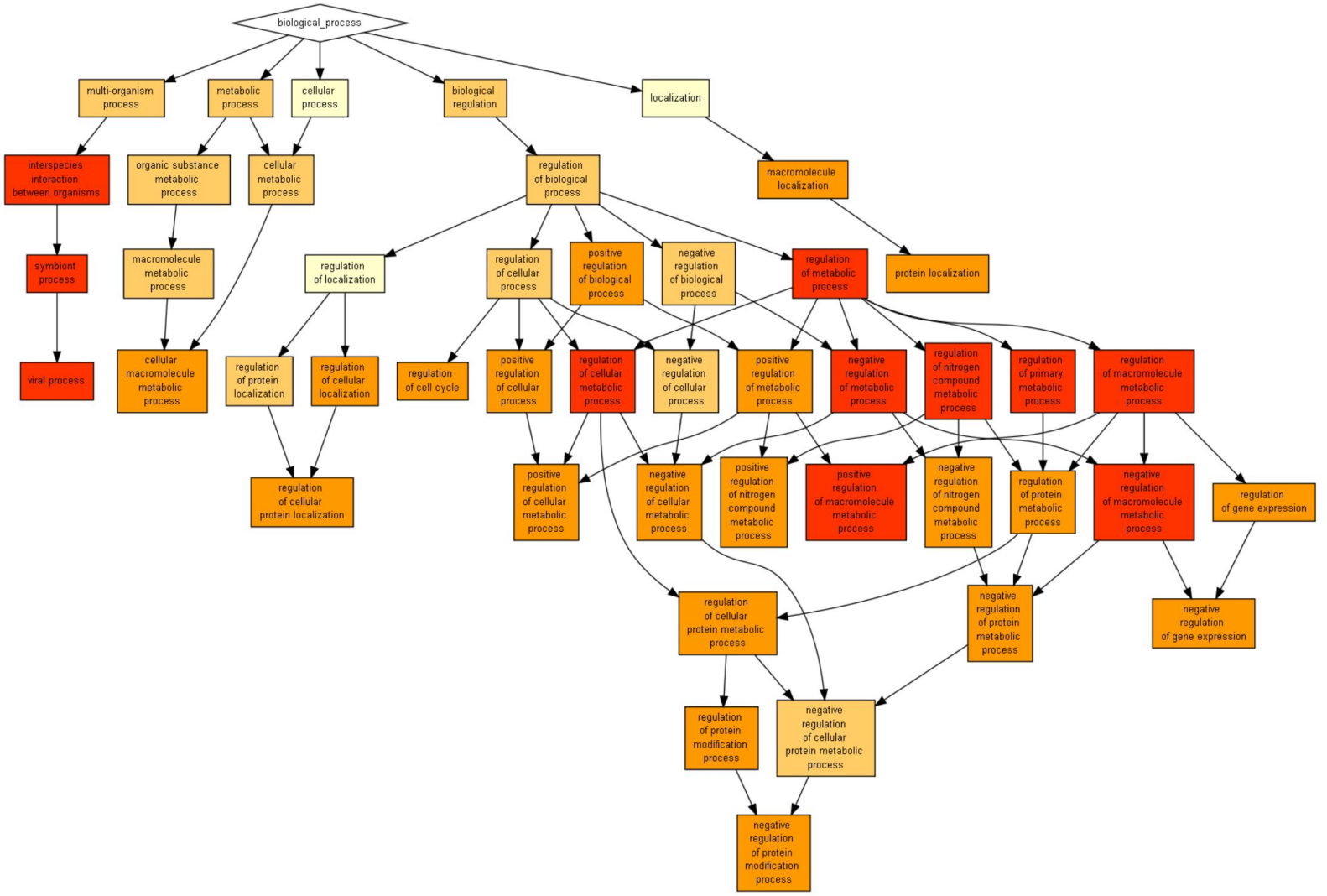
P value = 6.5×10^{-18}

Sigma – [8046, 478, 244]



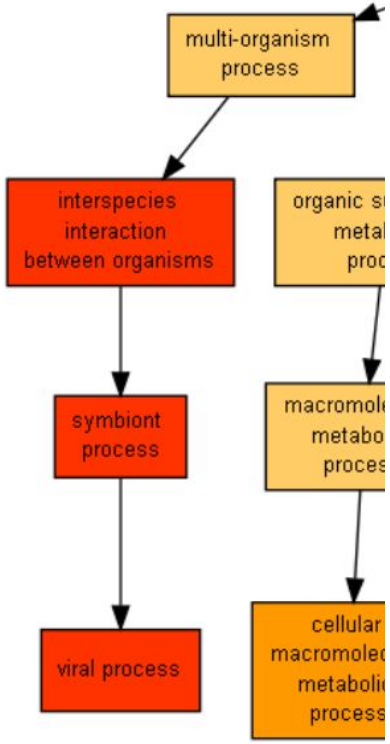
GOrilla Analysis of U – Overexpression in Women

- Column 2 of U sorted from smallest to largest
- Threshold of p-value set to 10^{-8}



GOrilla Analysis of U – Overexpression in Women

- 28/31 processes above this threshold were associated with metabolism or cell cycle regulation
- 3 genes highlighted are associated with viral reaction



	P-value	FDR q-value	Enrichment (N, B, n, b)
regulation of metabolic process	6.45E-13	9.66E-9	1.33 (11673,4890,817,455)
regulation of macromolecule metabolic process	2.42E-12	1.81E-8	1.35 (11673,4495,810,421)
regulation of cellular metabolic process	3.14E-12	1.57E-8	1.35 (11673,4513,817,425)
regulation of primary metabolic process	3.15E-12	1.18E-8	1.33 (11673,4422,810,407)
interspecies interaction between organisms	4.34E-12	1.3E-8	2.02 (11673,764,840,111)
regulation of nitrogen compound metabolic process	1.93E-11	4.82E-8	1.32 (11673,4290,810,394)
viral process	2.13E-11	4.55E-8	2.05 (11673,610,945,101)
symbiont process	2.13E-11	3.98E-8	2.05 (11673,610,945,101)
negative regulation of metabolic process	3.75E-11	6.24E-8	1.52 (11673,2230,808,234)
negative regulation of macromolecule metabolic process	3.86E-11	5.78E-8	1.55 (11673,2035,808,218)
positive regulation of macromolecule metabolic process	7.04E-10	9.58E-7	1.43 (11673,2677,810,265)
negative regulation of nitrogen compound metabolic process	1.18E-9	1.48E-6	1.54 (11673,1850,808,197)

- Data has suggested that HPV is the second most important etiological agent behind alone[1]
- HPV induced lung cancer has been more prevalent in women than men[1]

GOrilla Analysis of U – Overexpression in Men

- Column 2 of U sorted from largest to smallest
- Threshold of p-value set to 10^{-4}
- Most processes are associated with the membrane
  - Motility, cell-cell adhesion, protein localization, etc.

	P-value	FDR q-value	Enrichment (N, B, n, b)
epithelial cell-cell adhesion	2.04E-6	3.05E-2	8.88 (11673,12,876,8)
cardiac neural crest cell development involved in outflow tract morphogenesis	6.39E-6	4.78E-2	389.10 (11673,2,30,2)
establishment of protein localization to membrane	8.55E-6	4.27E-2	23.51 (11673,191,13,5)
negative regulation of locomotion	3.14E-5	1.17E-1	3.34 (11673,272,244,19)
protein localization to membrane	3.95E-5	1.18E-1	12.33 (11673,355,16,6)
negative regulation of cell motility	5.13E-5	1.28E-1	3.49 (11673,233,244,17)
apoptotic mitochondrial changes	6.05E-5	1.29E-1	18.53 (11673,45,70,5)
nucleocytoplasmic transport	6.31E-5	1.18E-1	3.14 (11673,206,343,19)
negative regulation of cellular component movement	6.54E-5	1.09E-1	3.30 (11673,261,244,18)
cellular protein-containing complex assembly	7.41E-5	1.11E-1	2.09 (11673,647,345,40)
protein targeting to membrane	7.86E-5	1.07E-1	30.96 (11673,116,13,4)
nuclear transport	7.96E-5	9.93E-2	3.09 (11673,209,343,19)
regulation of gene expression	8.04E-5	9.26E-2	1.33 (11673,3271,498,185)
SMAD protein complex assembly	9.43E-5	1.01E-1	18.06 (11673,6,431,4)
viral transcription	9.69E-5	9.67E-2	29.48 (11673,99,16,4)
negative regulation of cell migration	9.76E-5	9.13E-2	3.48 (11673,220,244,16)

Cell-Cell Adhesion:

NOV - nephroblastoma overexpressed
ITGB5 - integrin, beta 5
CTNNA1 - catenin (cadherin-associated protein), alpha 1, 102kda
KIFC3 - kinesin family member c3
VCL - vinculin
CYP1B1 - cytochrome p450, family 1, subfamily b, polypeptide 1
SRF - serum response factor (c-fos serum response element-binding transcription factor)
IHH - indian hedgehog

- CYP1A1 and CYP1B1 have previously been seen to be expressed at different levels in men and women[1]
- Evidence for link between estrogen and risk of lung cancer[1]

- Chikako Kiyohara. *Gender Medicine.* 7. 2010. pp. 381-401