

Doctoral Thesis

<Lung Precancer Analysis>

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## **Abstract**



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# **I Introduction**

## **1.1 Lung Cancer**

Lung cancer is the most common form of cancer as 12.3 % of all cancers (Minna, Roth, & Gazdar, 2002).

## **1.2 Non-small Cell lung cancer**

**Lung Adenocarcinoma (LUAD)**

**Lung Squamous Cell Carcinoma (LUSC)**

**LUSC vs. LUAD**

## **1.3 Lung Precancer**

## **1.4 Study Objectives**

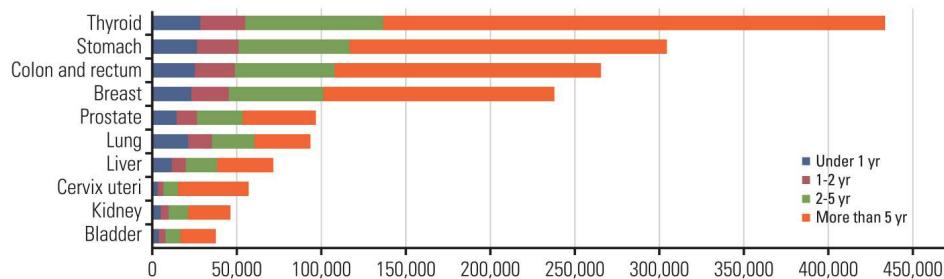


Figure 1: Common cancer survival rates (Hong et al., 2021)

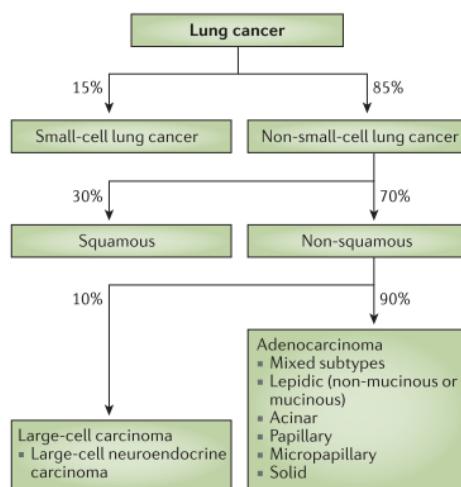


Figure 2: Lung cancer classification (Gridelli et al., 2015)

## **II Materials**

### **2.1 List of IPNs**

#### **Carcinoma *in situ***

Carcinoma *in situ* (CIS)

#### **Adenocarcinoma *in situ***

Adenocarcinoma *in situ* (AIS)

#### **Atypical Adenomatous Hyperplasia**

Atypical adenomatous hyperplasia (AAH)

#### **Dysplasia**

#### **Minimally Invasive Adenocarcinoma**

Minimally invasive adenocarcinoma (MIA)

### **2.2 Data Composition**

Table 1: WES Data Composition

Cancer Subtype	Stage	Number of Samples	
LUSC	Normal	77	
	Dysplasia	5	
	AAH	8	
	CIS+AIS	73	
	Primary	77	
	Total	240	
LUAD	Normal	18	
	AAH	15	
	CIS+AIS	9	
	MIA	1	
	Primary	18	
	Total	61	

Table 2: WTS Data Composition

Cancer Subtype	Stage	Number of Samples	
LUSC	Normal	17	
	Dysplasia	2	
	CIS+AIS	34	
	Primary	36	
	Total	89	
LUAD	Normal	13	
	AAH	1	
	CIS+AIS	5	
	Primary	6	
	Total	25	

### **III Methods**

#### **3.1 Workflows**

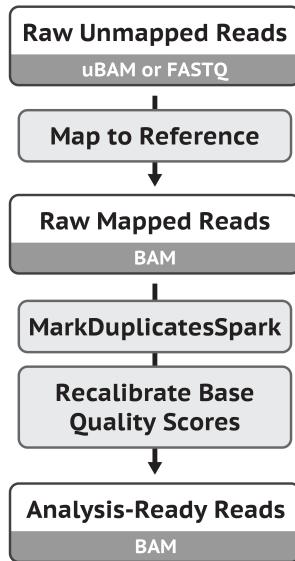


Figure 3: Workflow for data pre-processing for variant discovery (Van der Auwera et al., 2013; DePristo et al., 2011)

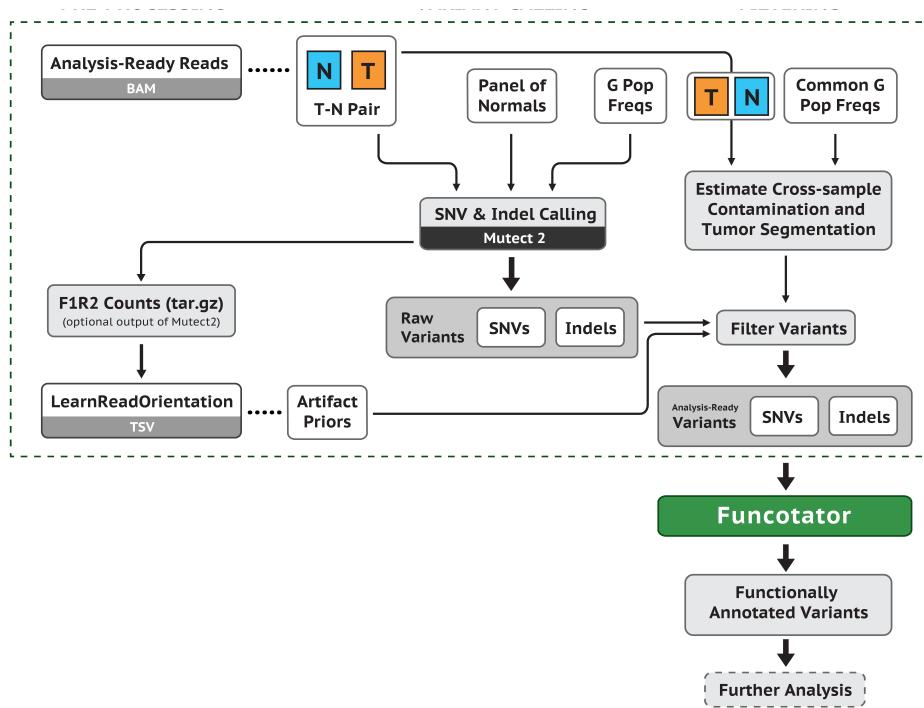


Figure 4: Somatic short variant discovery workflow (Van der Auwera et al., 2013; DePristo et al., 2011)

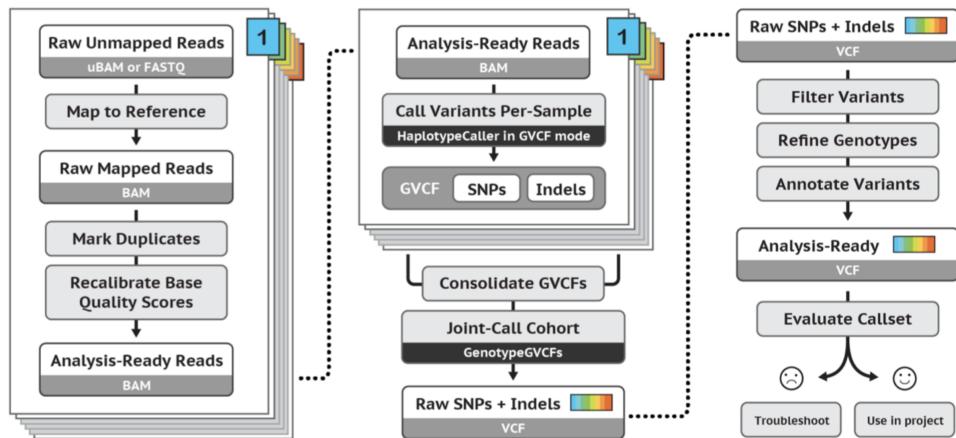


Figure 5: Germline short variant discovery workflow (Van der Auwera et al., 2013; DePristo et al., 2011)

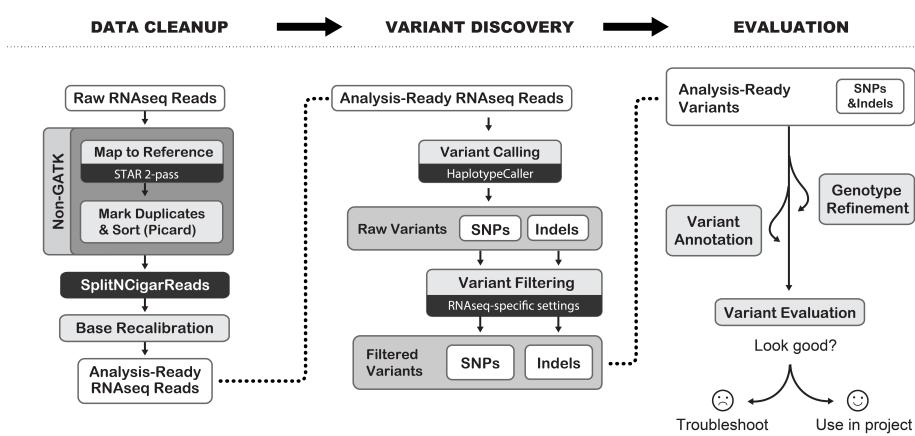


Figure 6: RNA-seq short variant discovery workflow (Van der Auwera et al., 2013; DePristo et al., 2011)

## **IV Results**

### **4.1 Quality Checks**

**Quality Checks with FastQC**

**Quality Checks with Depths**

**Quality Checks with Picard**

**Findings in Quality Checks**

### **4.2 Copy Number Variation Analyses**

**Purity and Ploidy**

**Copy Number Variation Plot**

**Findings in Copy Number Variation Analyses**

### **4.3 Single Nucleotide Variation Analyses**

**Somatic Short Variation Analyses with Mutect2**

**Somatic Short Variant with Clinical Data**

**Findings in Somatic Short Variation Analyses**

### **4.4 Variant Allele Frequency Analyses**

**Findings in Variant Allele Frequency Analyses**

### **4.5 Gene Fusion Analyses**

**Findings in Gene Fusion Analyses**

### **4.6 Differences in Gene Expression levels**

### **4.7 Bulk Cell Deconvolution Analyses**

**Single-cell Reference Data**

**GSE131907 as Reference**

**GSE162498 as Reference**

**GSE179994 as Reference**

**Findings in Bulk Cell Deconvolution Analyses**

### **4.8 Mutational Signature Analyses**

**Single Base Substitutions**

**Double Base Substitutions**

**Insertions and Deletions**

**Findings in Mutational Signature Analyses**

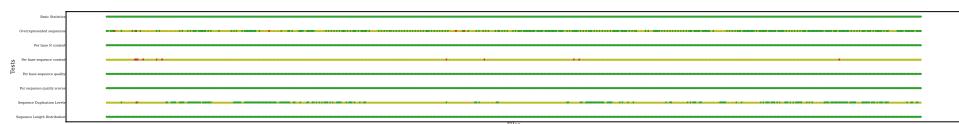


Figure 7: FastQC results with WES data

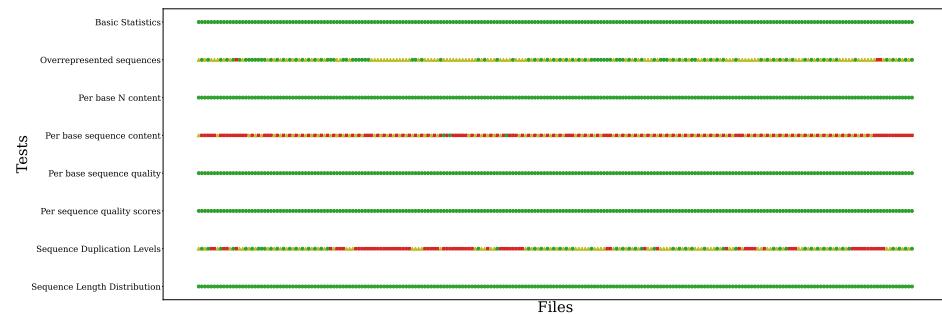


Figure 8: FastQC results with WTS data

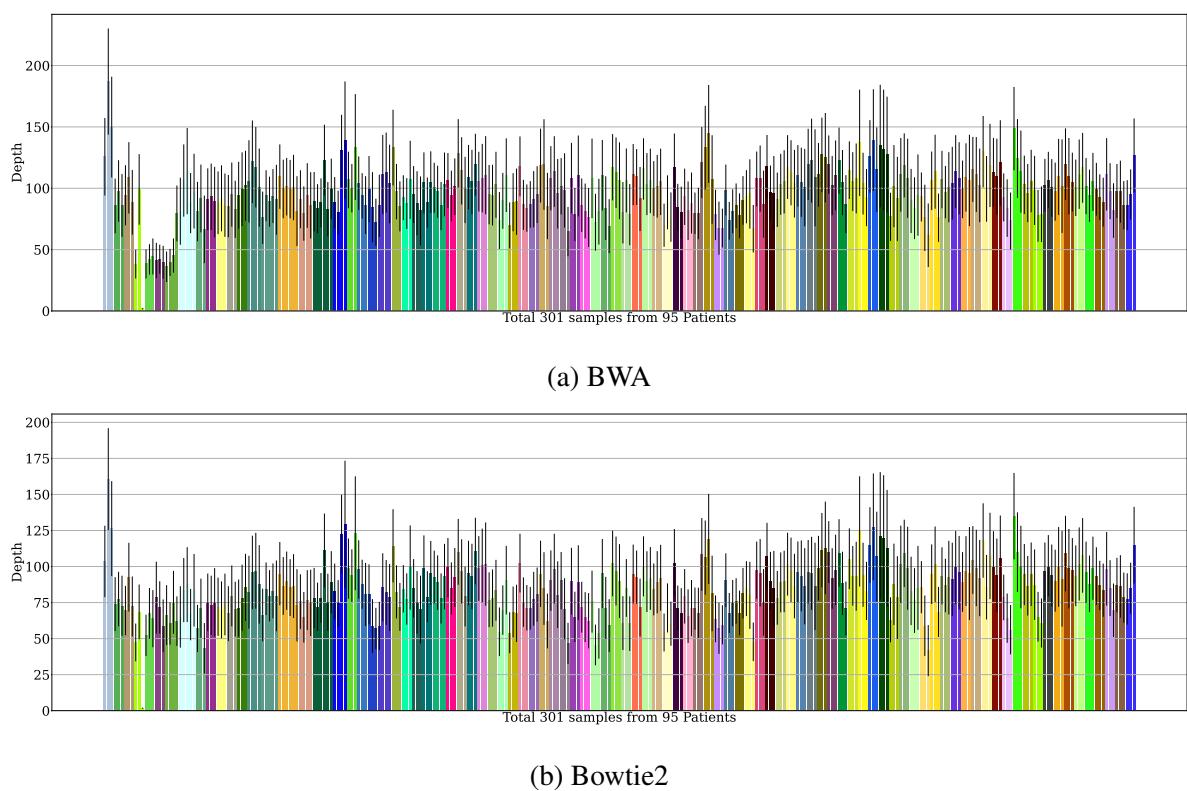
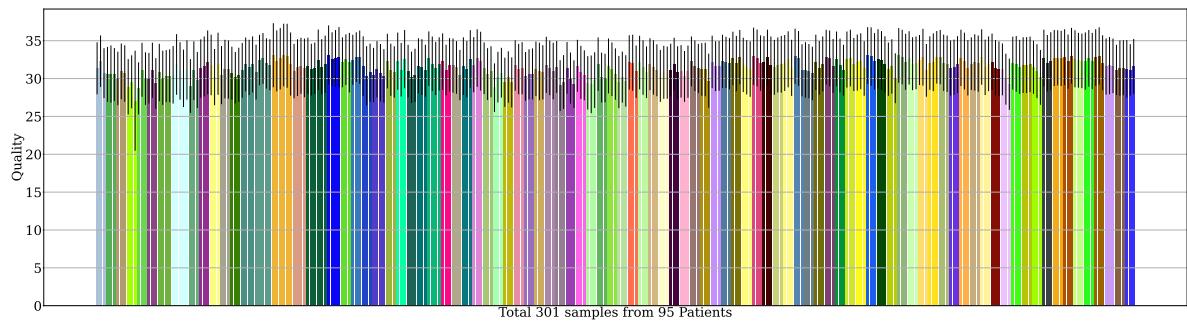
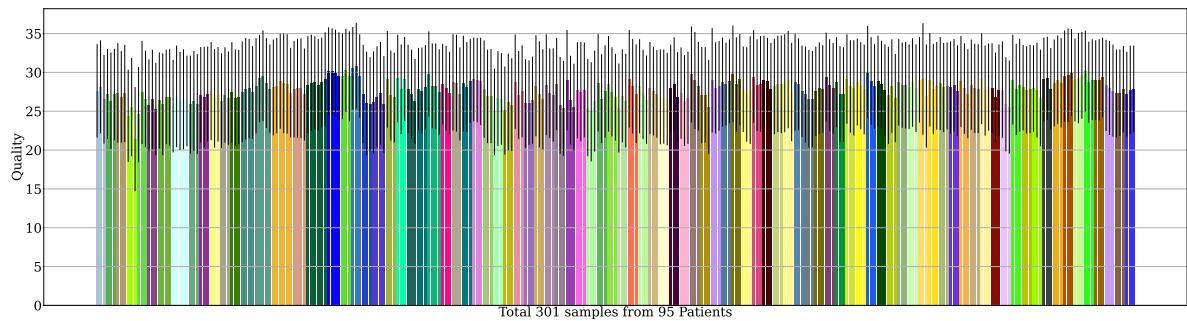


Figure 9: Depths plot with WES data



(a) BWA



(b) Bowtie2

Figure 10: Quality Distribution by Samples

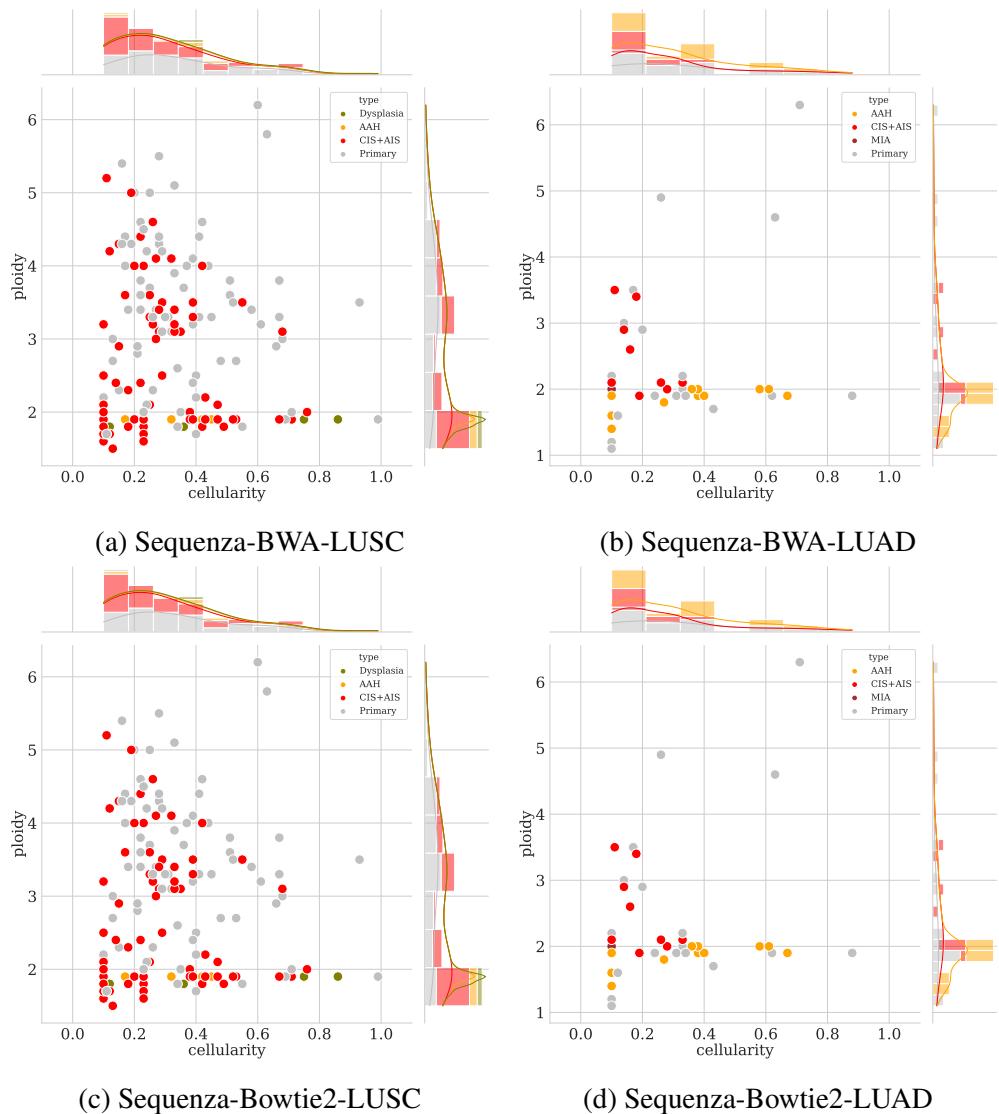


Figure 11: Sequenza Cellularity and Ploidy Plots

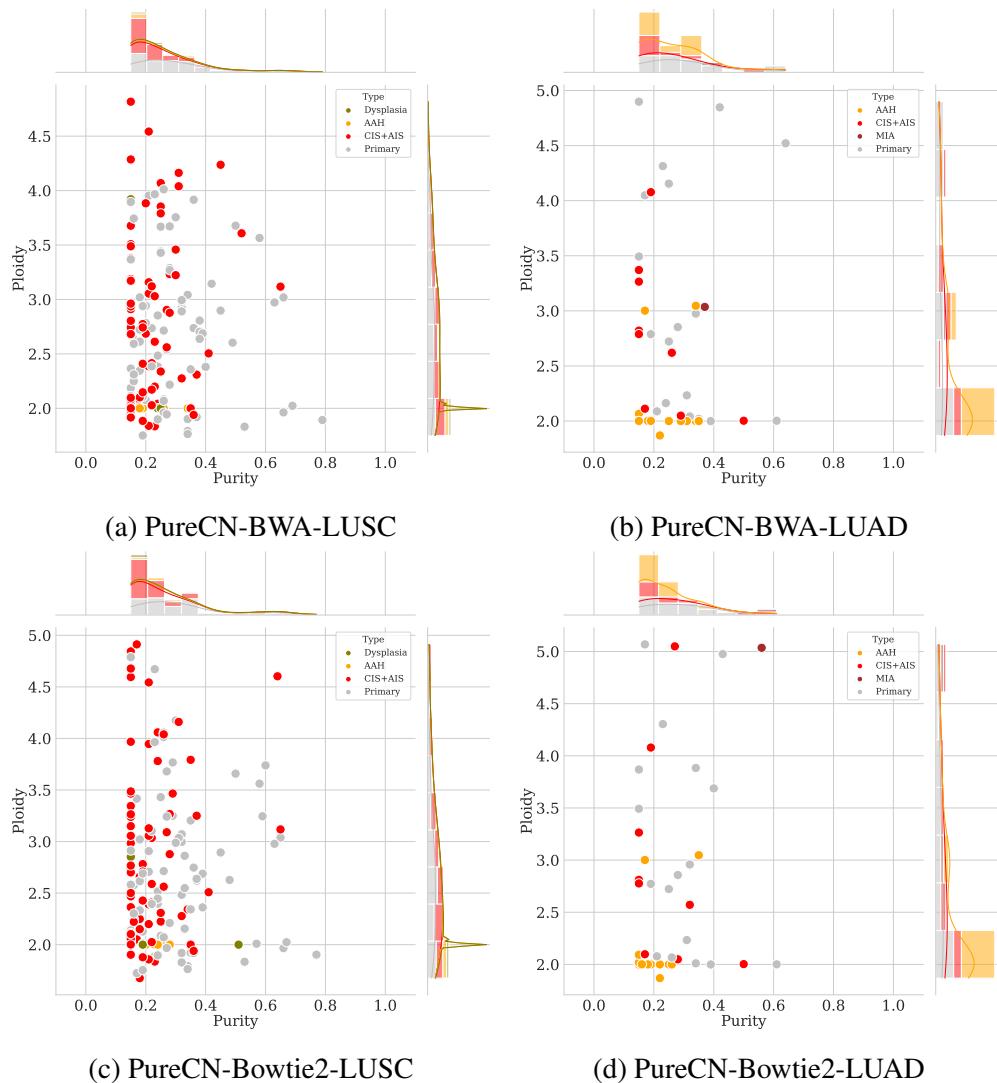


Figure 12: PureCN Purity and Ploidy Plots

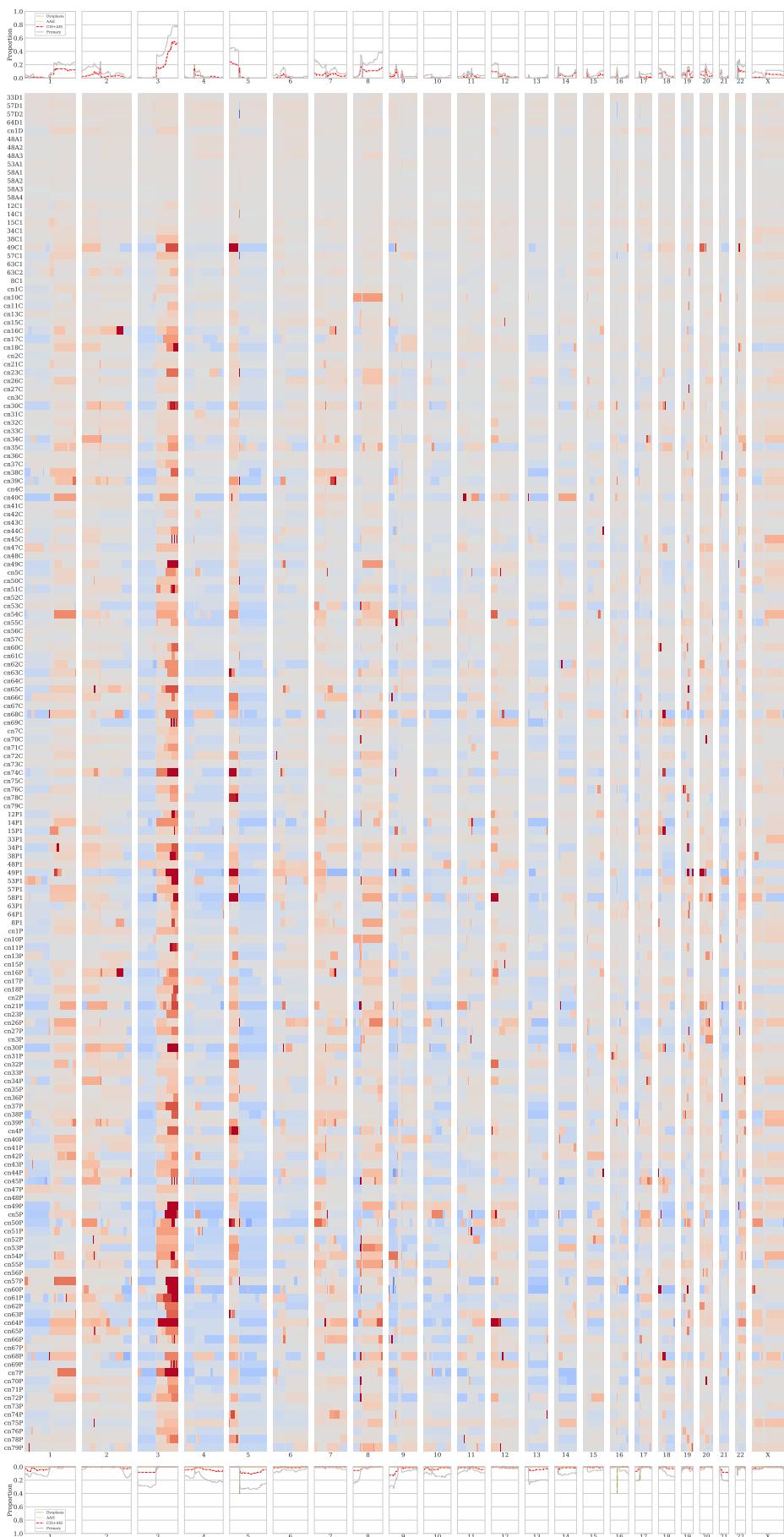


Figure 13: Sequenza LUSC Genome View Plot  
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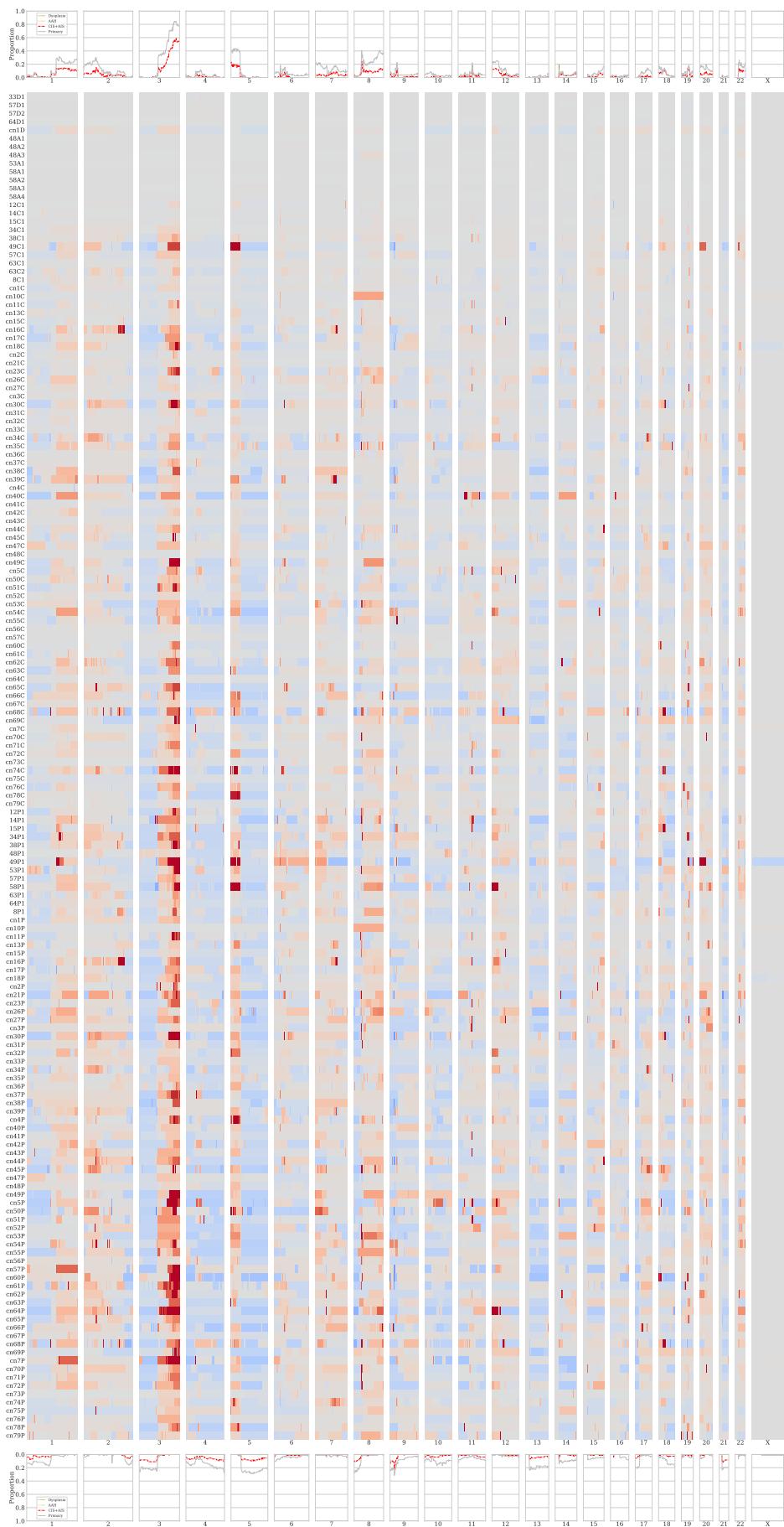


Figure 14: PureCN LUSC Genome View Plot  
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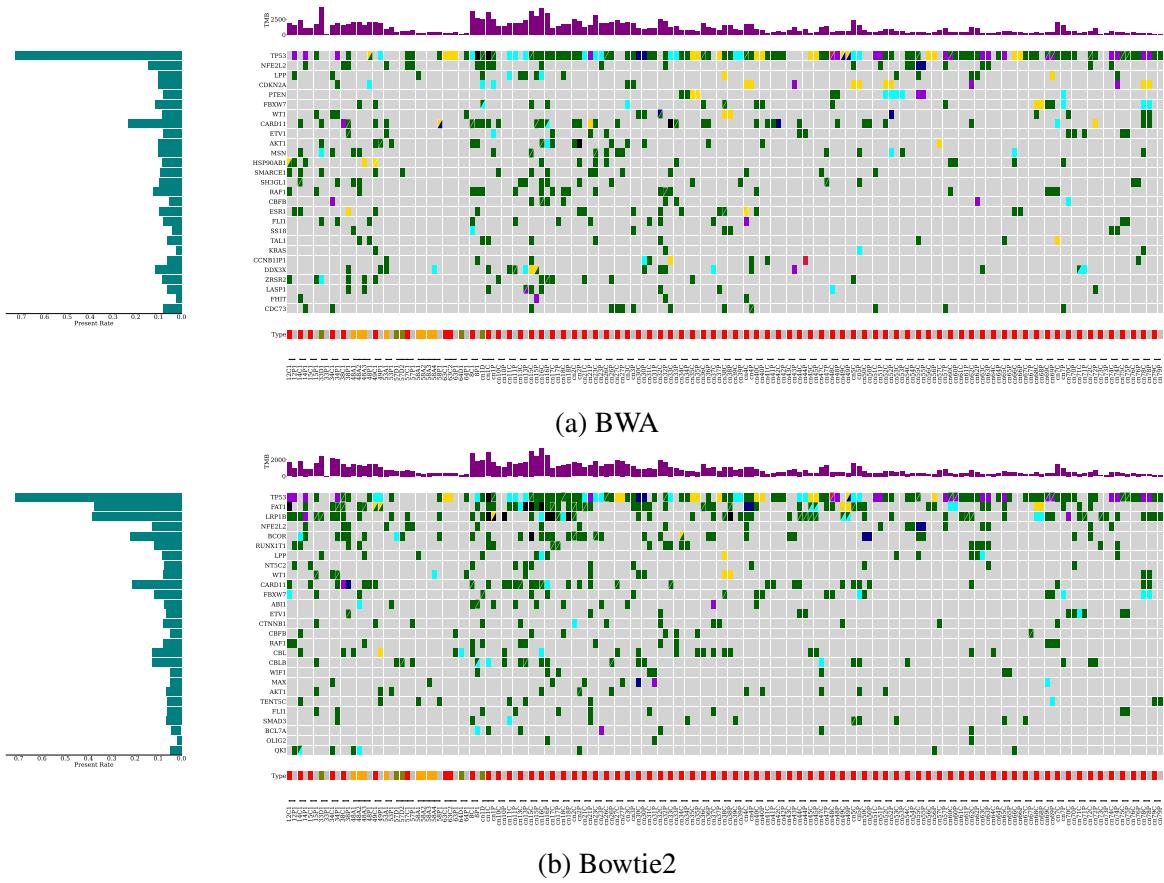


Figure 15: Comut Plot by LUSC

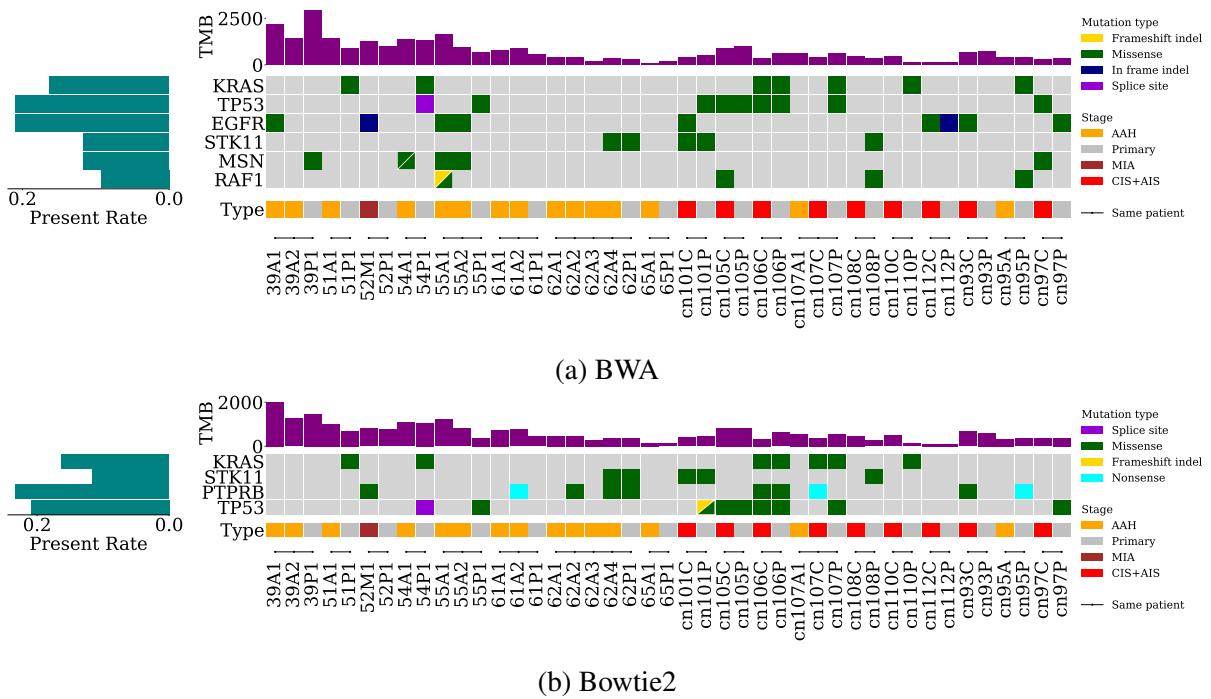


Figure 16: Comut Plot by LUAD

## **V Discussion**

**5.1 General Conclusions**

**5.2 Plan for Future**

**5.3 Future Perspective**

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## **Acknowledgements**

Thank you very much.

