# Adrenal Cancer Case Study

Jaidev Menon



Examine different prognostic markers and patient demographics with three common forms of adrenal cancer in order to determine which factors contribute to increased disease mortality and reduced survival time

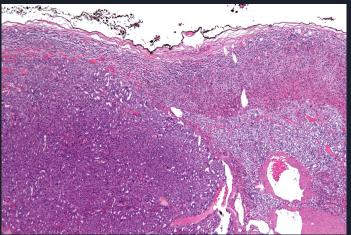
## Adrenal Gland Tumors

- 1. Adrenocortical Carcinoma
- 2. Pheochromocytoma/Paraganglioma
- 3. Neuroblastoma

## Adrenocortical Carcinoma

- Tumor that originates from the adrenal cortex.
- Most common type of adrenal cancer with common malignancy. 50% survival rate
- May overproduce hormones such as aldosterone, cortisol, estrogen and testosterone
- Symptoms: abdominal pain, hirsutism, gynecomastia, high BP, high blood sugar
- Complications: Cushing's syndrome from high cortisol production, Conn's syndrome from high aldosterone production
- Treatment: adrenalectomy





## Dataset

Diagnosis Age Diagnosis Age Range Prior Diagnosis Aneuploidy Score MSI\_MANTIS\_Score MSIsensor Score Mutation Count

10.0

12.0

17.0

33.0

22.0

24.0

7.0

27.0

33.0

13.0

28.0

39.0

21.0

18.0

39.0

Tumor Break Load Overall Survival Months Survival Status Radiation Therapy Tumor Progression or Recurrence

45.0 Dead w/ Tumor

55.0 Dead w/ Tumor

69.0 Alive w/ Tumor

14.0 Dead w/ Tumor

12.0 Dead w/ Tumor

16.0 Dead w/ Tumor

19.0 Dead w/ Tumor

44.0 Alive w/ Tumor

30.0 Dead w/ Tumor

18.0 Alive Tumor-Free

58.0 Alive Tumor-Free

69.0 Dead w/ Tumor

100 0 Alive Tumor-Free No

66.0 Alive Tumor-Free Yes

89.0 Alive Tumor-Free No.

0.28

0.32

0.34

0.3

0.52

0.29

0.29

0.32

0.32

0.31

0.29

0.3

0.3

0.29

0.29

0.32

Recurrence

Recurrence

Recurrence

Recurrence

Recurrence

Recurrence

Recurrence

Recurrence

Progression

Neither

Neither

Neither

Neither

Recurrence

Neither

1.57

1.82

0.45

5.38

0.0

0.79

0.64

0.9

0.72

0.35

0.56

0.46

0.0

0.91

1.45

29.0

10.0

116.0

354.0

30.0

48.0

89.0

31.0

477.0

280.0

27.0

26.0

52.0

66.0

26.0

OR-A5J1

OR-A5J2

2 OR-A5J3

3 OR-A5J4

5 OR-A5J6

OR-A5J5

OR-A5J7

OR-A5J8

OR-A5J9

9 OR-A5JA

10 OR-A5JB

11 OR-A5JC

12 OR-A5JD

13 OR-A5JE

14 OR-A5JF

15 OR-A5JG

Female Hispanic

Female Hispanic

Female Hispanic

Female Hispanic

Female White

Female White

5.85 0.8

40.33 0.97

41.31 0.33

92.59

47.85

89.33

25.28 2.97

94.66

79.04 15.77

33.72

65.36

94.77 0.87

> 49.1 1.73

90.14

80.15 11.87

3.87

1.0

1.6

1.03

9.4

0.9

2.2

Percent Genome Altered TMB

Hispanic

Hispanic

58 51-70

44 31-50

23 14-30

23 14-30

30 14-30

29 14-30

30 14-30

66 51-70

22 14-30

53 51-70

52 51-70

37 31-50

57 51-70

17 14-30

69 51-70

61 51-70

421.0

68.0

7.0

474.0

36.0

12.0

384.0

186.0

106.0

162.0

84.0

172.0

40

177.0

38.0

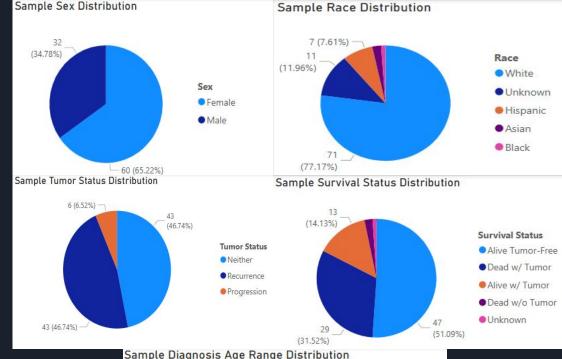
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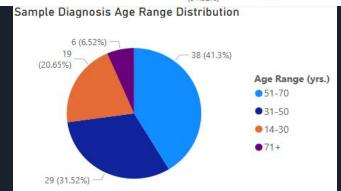
- Published by The Cancer Genome Atlas (TCGA) in 2021
- Analyzes the tumor samples of 92 patients

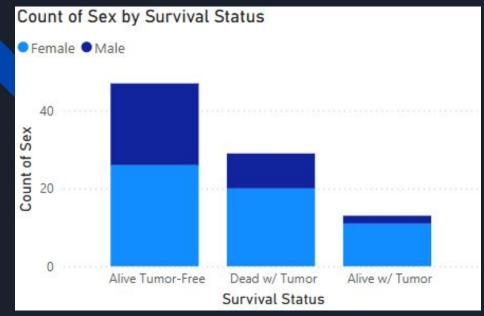
  - Aneuploidy Score: number of altered chromosome arms ranging from 0 to 39. High score may indicate reduced
  - response to immunotherapy
- Mutation Count: high score may indicate tumor progression
- % Genome Altered: high % increase likelihood of malignancy
- MSI Mantis Score: measurement of microsatellite (MSI)
- instability that predicts likelihood of high MSI
- MSISensor Score: % indicates likelihood of MSI instability
- Tumor mutational burden (TMB): number of genetic
- mutations in a tumor's DNA
- Tumor break load: measure of genomic instability by adding up all unbalanced chromosomal breaks in a tumor

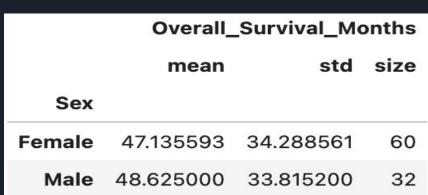
## Demographics

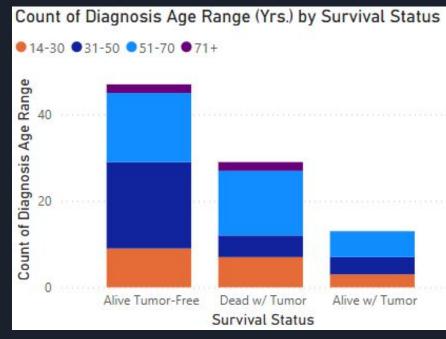
- Dataset is mostly White
- Many instances of tumor recurrence but little progression
- Most patients are either alive tumor-free or dead from tumor
- Diagnosis age most commonly 51-70 years
- Patient prognosis will be determined by survival status and months of survival after diagnosis





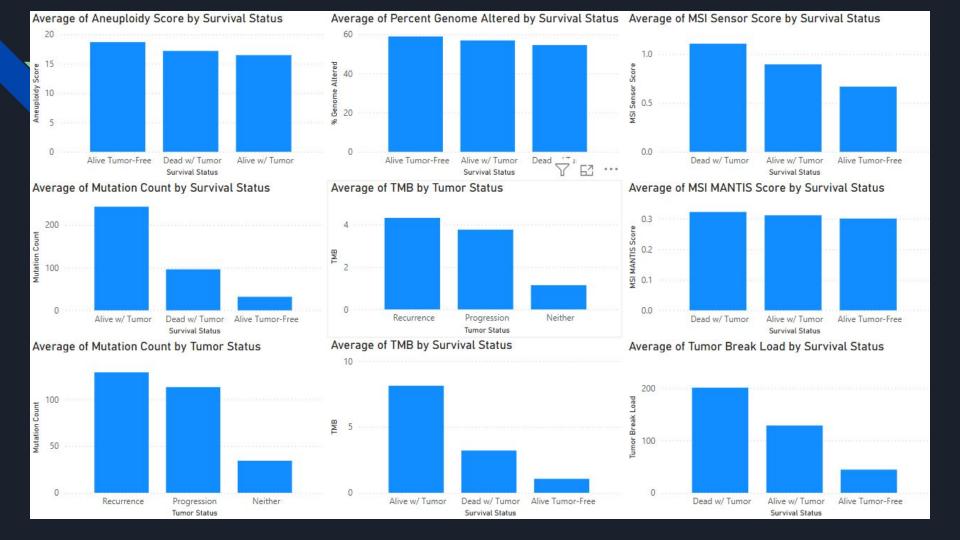






	Overall_	_Survival_Mo	nths	t-test	p-value
	mean	std			
Diagnosis Age Range					
14-30	46.684211	32.567968	19	-0.13	0.900
31-50	59.750000	36.350786	29	1.79	0.077
51-70	39.894737	32.079959	38	-1.49	0.140
71+	43.500000	29.432975	6	-0.35	0.730





## Analysis

- No significant variance in survival length based on sex or diagnosis age range. Diagnosis age 31-50 has a slightly higher survival length
- Mutation Count and TMB and MSI Mantis Score and MSISensor Score are highly positively correlated
- Aneuploidy Score and Percent Genome Altered are moderately positively correlated
- Tumor Break Load is significantly different between alive w/o tumor, alive w/ tumor and dead w/ tumor
- Mutation count and TMB are significantly different between alive w/o tumor and dead w/ tumor

		Mutat	ion Count	Percent_	_Genome_A	Itered	Α	neuploidy S	core
		mean	std	m	ean	std	mean	std	size
Survival Statu	s								7
Alive Tumor-Fre	<b>e</b> 31.7	17391 4	48.994178	58.924	222 33.3	09868 1	8.688889	11.367462	47
Alive w/ Tumo	r 242.53	8462 54	49.536716	56.901	538 31.2	90767 1	6.461538	9.700648	13
Dead w/ Tumo	r 96.00	00000 1	18.748835	54.540	000 27.4	28044	17.178571	9.185551	29
	MSI_MAN	TIS_Score	MSIsen	sor Score	Tumoi	Break Loa	d		ТМВ
	MSI_MAN mean	TIS_Score std	MSIsen mean	sor Score	Tumoi mean	Break Loa		ı std	TMB size
Survival Status		_						ı std	
Survival Status Alive Tumor-Free		_					d mear		
	mean	std	mean 0.666087	std	mean	st	nd mear 11 1.059783	3 1.643193	size

	Mutation Count ttest/p-value	Percent Genome Altered ttest/p-value	Aneuploidy Score ttest/p-value	MSI Mantis Score ttest/p-value	MSIsensor Score ttest/p-value	Tumor Break Load ttest/p-value	TMB ttest/pvalue
Alive w/ Tumor vs Alive Tumor-Free	1.38/0.10	-0.20/0.58	-0.71/0.76	0.05/0.48	0.61/0.28	3.36/<0.01	1.38/0.10
Dead w/ Tumor vs Alive w/ Tumor	-0.95/0.82	-0.23/0.59	0.23/0.41	0.32/0.38	0.46/0.32	1.72/0.046	-0.95/0.82
Dead w/ Tumor vs Alive Tumor-Free	2.773/<0.01	-0.62/0.73	-0.63/0.74	1.64/0.056	1.33/0.096	4.45/<0.01	2.78/<0.01

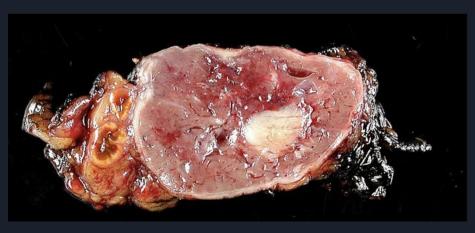
# Pheochromocytoma vs Paraganglioma

#### **Pheochromocytoma**

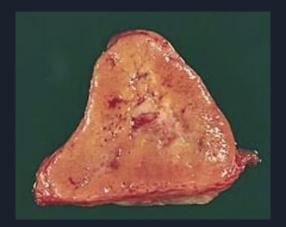
- Most common adrenal medulla tumor in adults derived from chromaffin cells of neural crest. Can cause overproduction of dopamine, norepinephrine, epinephrine and EPO
- Symptoms: hyperadrenergic sx of increased BP, headaches, sweating, increased HR and pallor
- Mostly benign. Extra-adrenal, bilateral and/or malignant around 10% of the time.
- Treatment: alpha-antagonists followed by beta blockers

#### **Paraganglioma**

- Neuroendocrine tumor also derived from chromaffin cells.
   Located near blood vessels and nerves around the body
- Symptoms: asymptomatic or same sx as pheochromocytoma
- Mostly benign, but higher chance of malignancy than pheochromocytoma due to its anatomic location
- Treatment: surgery or same tx as pheochromocytoma



Pheochromocytoma



Paraganglioma

#### Dataset

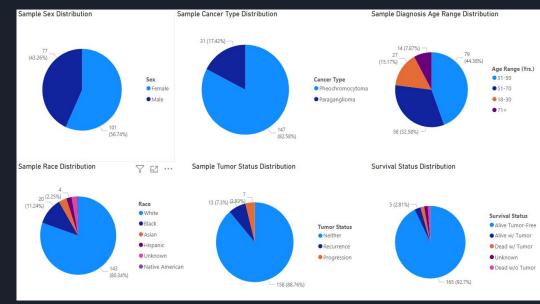
- Published by the Cancer Genome Atlas in 2013
- Analyzes pheochromocytoma and paraganglioma tumor samples of 178 patients
- Same diagnostic measures as adrenocortical carcinoma dataset
- Hypoxia Score: calculates the gene expression of hypoxia to estimate how much hypoxia is present in a patient. Buffa, Ragnum and Winter scores specifically measure hypoxia in tumors

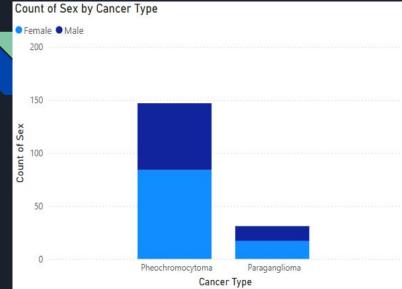
	Patient_ID	Cancer Type Detailed	Sex	Race	Diagnosis Age	Diagnosis Age Range	Prior Diagnosis	Aneuploidy Score	Buffa Hypoxia Score	Ragnum Hypoxia Score	Winter Hypoxia Score
0	P7-A5NX	Pheochromocytoma	Female	Hispanic	78	71	No		-19	-20	-34
1	P7-A5NY	Pheochromocytoma	Female	White	21	18-30	Yes	2.0	-19	-10	-36
2	P8-A5KC	Pheochromocytoma	Male	White	48	31-50	No	0.0	-21	-26	-46
3	P8-A5KD	Pheochromocytoma	Female	White	35	31-50	No	9.0	-33	-14	-44
4	P8-A6RX	Paraganglioma	Male	White	65	51-70	No	6.0	13	-8	-18
5	P8-A6RY	Pheochromocytoma	Male	White	55	51-70	No	3.0	-23	-22	-40
6	PR-A5PF	Pheochromocytoma	Female	White	62	51-70	No	8.0	-19	-22	-40
7	PR-A5PG	Pheochromocytoma	Female	White	42	31-50	No	5.0	-23	-16	-34
8	PR-A5PH	Pheochromocytoma	Male	White	47	31-50	No	2.0	-21	-22	-44
9	QR-A6GO	Pheochromocytoma	Male	White	43	31-50	No	6.0	-15	-18	-16
10	QR-A6GR	Pheochromocytoma	Female	White	30	18-30	No	2.0	-9	-24	-18
11	QR-A6GS	Pheochromocytoma	Female	White	51	51-70	No	2.0	-33	-24	-38
12	QR-A6GT	Pheochromocytoma	Female	White	63	51-70	No	6.0	-1	-16	-6
13	QR-A6GU	Pheochromocytoma	Male	White	31	31-50	No	5.0	-13	-16	-32
14	QR-A6GW	Pheochromocytoma	Female	White	53	51-70	No		-11	-18	-22
15	QR-A6GX	Pheochromocytoma	Female	Black	28	18-30	No	20.0	-17	-18	-36
16	QR-A6GY	Pheochromocytoma	Female	White	37	31-50	No	5.0	-13	-20	-24
17	QR-A6GZ	Pheochromocytoma	Male	White	31	31-50	Yes	23.0	13	-10	-2
18	QR-A6H0	Paraganglioma	Male	White	53	51-70	No	2.0	-13	-22	-32
19	QR-A6H1	Pheochromocytoma	Male	White	55	51-70	Yes	5.0	-5	-18	-22
20	QR-A6H2	Pheochromocytoma	Male	Asian	33	31-50	No	1.0	-7	-20	-10

MSI_MANTIS_Score	MSIsensor Score	<b>Mutation Count</b>	Percent_Genome_Altered	тмв	Tumor Break Load	Overall_Survival_Months	Survival Status	Radiation Therapy	Tumor Progression or Recurrence
0.35	0.0	17		0.57	45.0	27.0	Alive Tumor-Free	No	Neither
0.36	0.03	6	7.51	0.2	2.0	31.0	Alive Tumor-Free	No	Neither
0.32	0.02	11	0.04	0.73	20.0	29.0	Alive Tumor-Free	No	Neither
0.33	0.0	7	21.75	0.47	4.0	4.0	Alive Tumor-Free	No	Neither
0.36	0.06	20	23.55	0.67	20.0	18.0	Alive Tumor-Free	No	Neither
0.32	0.0	4	5.71	0.13	0.0	6.0	Alive Tumor-Free	No	Neither
0.36	0.02	16	20.69	0.53	43.0	18.0	Alive Tumor-Free	No	Neither
0.37	0.03	15	13.6	0.5	9.0	82.0	Alive Tumor-Free	No	Recurrence
0.36	0.0	8	7.25	0.27	29.0	28.0	Alive Tumor-Free	No	Neither
0.36	0.0	11	10.7	0.37	7.0	35.0	Alive Tumor-Free	No	Neither
0.31	0.0	12	6.49	0.37	59.0	23.0	Alive Tumor-Free	No	Neither
0.32	0.0	9	7.2	0.3	37.0	1.0	Alive Tumor-Free	No	Neither
0.33	0.04	24	20.96	0.83	3.0	138.0	Alive w/ Tumor	No	Recurrence
0.32	0.02	17	12.06	0.57	4.0	59.0	Alive Tumor-Free	No	Neither
0.35	0.06	16		0.53		16.0	Alive Tumor-Free	No	Neither
0.35	0.02	12	44.2	0.4	6.0	19.0	Alive Tumor-Free	No	Neither
0.36	0.03	16	11.13	0.53	17.0	1.0	Alive Tumor-Free	No	Neither
0.34	0.0	4	12.23	0.13	15.0	31.0	Alive Tumor-Free	No	Neither
0.32	0.0	4	6.79	0.13	2.0	9.0	Alive Tumor-Free	No	Neither
0.32	0.0	14	12.86	0.47	5.0	14.0	Alive Tumor-Free	No	Neither
0.33	0.0	8	5.37	0.27	6.0	10.0	Alive Tumor-Free	No	Neither

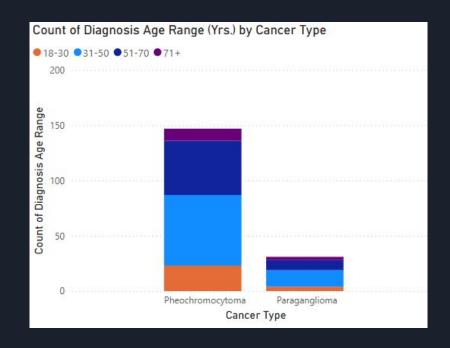
## Demographics

- Dataset is mostly White
- Most patients do not experience tumor recurrence or progression and end up alive tumor-free.
- Relatively even distribution of sex.
- Most pt's are between 51-70 years old
- Since survival and tumor status are skewed in sample population, pheochromocytoma vs paraganglioma will be assessed to determine patient prognosis
- Paraganglioma considered deadlier than pheochromocytoma due to its higher chance of metastasis

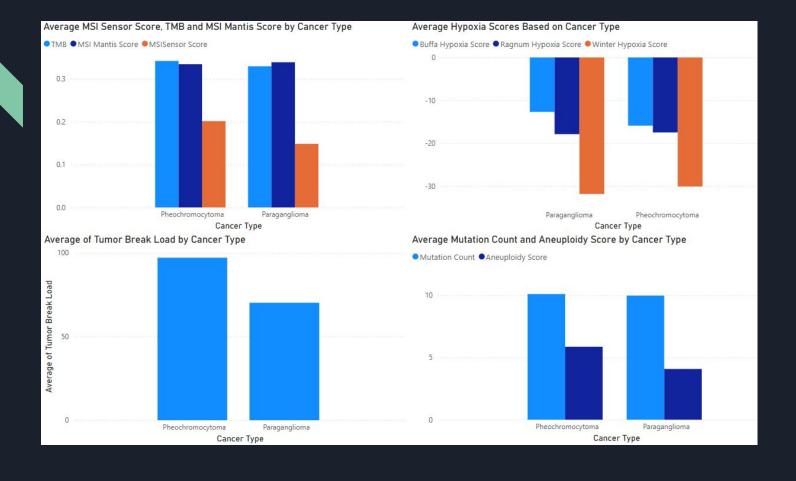




	Female	Male
Proportion of Paraganglioma	16.8%	18.2%
Size	101	77



	18-30	31-50	51-70	71+
Percentage of Paraganglioma	17.4%	19%	15.52%	27.3%
Size	27	79	58	14
Paraganglioma vs Pheochromocytoma Z-test	-0.004	-0.363	-0.674	0.793
p-value	0.5	0.64	0.75	0.21
Statistically Significant?	No	No	No	No



## Analysis

- No significant variance in sex or diagnosis age range between paraganglioma and pheochromocytoma
- Percent Genome Altered and Aneuploidy Score is almost significantly lower in paraganglioma compared to pheochromocytoma.
- No statistically significant difference between pheochromocytoma and paraganglioma in regards to mutation count, MSI MANTIS Score, MSIsensor score, tumor break load, TMB and Buffa, Ragnum and Winter Hypoxia Scores

	Mutation Count		nt Percent_Genome_Altered Ane		Aneuple	neuploidy Score MSI_MANTIS_Sc			e MSIsensor Score		
	mean	std	mean	mean std r		std	mean	std	mean	std	size
Cancer Type Detailed											
Paraganglioma	9.967742	5.480170	11.451111	7.508529	4.074074	2.540835	0.338710	0.018210	0.014839	0.023787	31
Pheochromocytoma	10.095238	5.531149	16.559104	14.838975	5.857143	5.484334	0.334218	0.015916	0.020136	0.036621	147

		Tumo	Tumor Break Load			Buffa Hyp	Buffa Hypoxia Score Ragnum Hypoxia Scor			Winter Hypoxia Score		
		mean	std	mean	std	mean	std	mean	std	mean	std	size
(	Cancer Type Detailed											
	Paraganglioma	70.161290	165.519605	0.329355	0.183538	-12.677419	11.052563	-17.870968	4.410154	-31.806452	11.504838	31
	Pheochromocytoma	97.075342	334.951342	0.341769	0.187433	-15.884354	11.189842	-17.469388	4.196062	-30.054422	12.872282	147

	Mutation Count	Percent Genome Altered	Aneuploidy Score	MSI Mantis Score	MSIsensor Score	Tumor Break Load	ТМВ	Buffa Hypoxia Score	Ragnum Hypoxia Score	Winter Hypoxia Score
Paraganglioma vs Pheochromocytoma t-test	-0.12	-1.86	-1.8	1.39	-0.72	-0.44	-0.27	1.45	-0.48	-0.7
p-value	0.91	0.064	0.08	0.165	0.47	0.66	0.79	0.15	0.63	0.48
Statistically Significant?	No	~No	~No	No	No	No	No	No	No	No

#### Neuroblastoma

- Most common tumor of adrenal medulla in children that originates from neural crest cells
- Symptoms: abdominal distension and mass that crosses midline, unlike Wilms tumor, opsoclonus-myoclonus syndrome
- Poor prognosis w/ earlier diagnosis having a higher chance of survival
- Treatment: Surgery and chemotherapy



#### Dataset

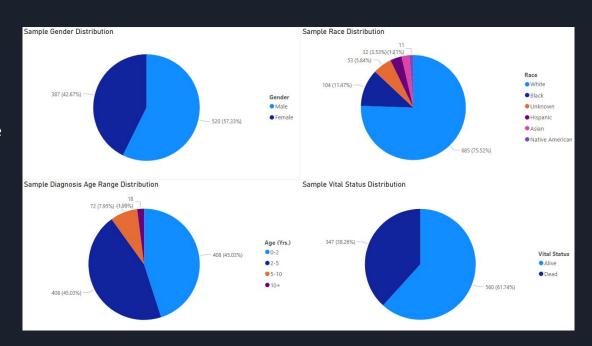
- Published by Therapeutically Applicable Research to Generate Effective Treatments (TARGET) program by National Cancer Institute in 2015
- Contains 907 tumor samples of patients
- MYCN Status: determines the amplification/ expression of MYCN gene in neuroblastomas
- Diploid or Hyperdiploid: Diploid has a normal 2 sets of chromosomes, whereas hyperdiploid indicates an abnormal higher number of chromosomes
- Histology: Favorable histology has normal looking tissue under microscope, unfavorable has abnormal tissue
- MKI: number of mitotic nuclei and karyorrhectic nuclei per 5,000 neuroblastic cells. Higher number indicates a more aggressive tumor

	target_usi	Gender	Nationality	Age at Diagnosis in Weeks	Diagnosis Age Range in Years	Year of Diagnosis	Year of Last Follow Up
12	PADFLI	Male	White	80.0	0-2	1991	1999.0
15	PADIHC	Male	White	274.0	5-10	1992	2005.0
16	PADINC	Male	Black	143.0	2-5	1992	1993.0
17	PADIRB	Female	Unknown	170.0	2-5	1992	2003.0
20	PADKGF	Male	White	79.0	0-2	1992	2000.0
21	PADKNE	Female	White	250.0	2-5	1993	1994.0
22	PADKRU	Female	White	204.0	2-5	1993	1994.0
24	PADKXS	Female	White	93.0	0-2	1993	1994.0
25	PADKYP	Male	White	246.0	2-5	1993	1996.0
26	PADLDA	Male	White	656.0	10	1993	1995.0
27	PADLDT	Female	White	115.0	2-5	1993	1993.0
28	PADLES	Female	White	255.0	2-5	1993	1996.0
29	PADLIC	Male	White	262.0	5-10	1993	2006.0
31	PADLKJ	Male	White	111.0	2-5	1993	1998.0
32	PADLNM	Male	Hispanic	135.0	2-5	1993	1994.0
33	PADLPR	Male	Black	115.0	2-5	1993	1994.0
35	PADLTD	Female	Hispanic	136.0	2-5	1993	1994.0
37	PADMTD	Male	White	149.0	2-5	1993	2002.0
39	PADMXD	Male	White	155.0	2-5	1993	1999.0
40	PADMYD	Male	White	218.0	2-5	1993	1994.0

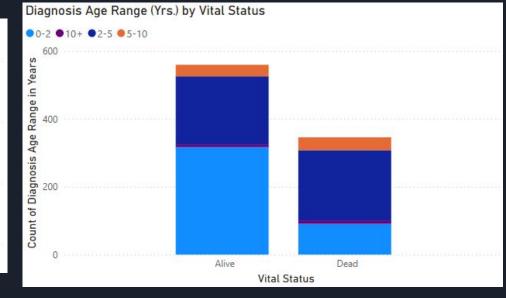
MYCN status	Diploid or Hyperdiploid	Histology	Tumor_Grade	мкі	Survival Time in Weeks	Vital Status
Not Amplified	Unknown	Unfavorable	3-4	High	410.0	Alive
Not Amplified	Unknown	Unfavorable	3-4	Low	657.0	Alive
Amplified	Unknown	Unfavorable	3-4	Low	58.0	Dead
Not Amplified	Unknown	Unfavorable	3-4	Low	551.0	Alive
Not Amplified	Unknown	Unfavorable	3-4	High	378.0	Alive
Amplified	Unknown	Unfavorable	3-4	High	84.0	Dead
Not Amplified	Unknown	Unfavorable	3-4	Intermediate	89.0	Dead
Amplified	Unknown	Unfavorable	3-4	Low	49.0	Dead
Amplified	Unknown	Unfavorable	3-4	High	155.0	Dead
Not Amplified	Unknown	Unfavorable	3-4	Low	113.0	Dead
Amplified	Unknown	Unfavorable	3-4	Intermediate	2.0	Dead
Not Amplified	Unknown	Unfavorable	3-4	Intermediate	192.0	Dead
Not Amplified	Unknown	Unfavorable	3-4	High	667.0	Alive
Amplified	Unknown	Unknown	Unknown	Unknown	250.0	Alive
Amplified	Unknown	Unfavorable	3-4	High	65.0	Dead
Not Amplified	Unknown	Unfavorable	3-4	Low	63.0	Dead
Amplified	Unknown	Unfavorable	3-4	Intermediate	68.0	Dead
Amplified	Unknown	Unfavorable	3-4	High	462.0	Alive
Amplified	Unknown	Unfavorable	3-4	High	293.0	Alive
Not Amplified	Unknown	Unfavorable	3-4	Intermediate	63.0	Dead

## Demographics

- Dataset is mostly White
- Relatively even distribution of Gender and Vital Status
- Most patients are in diagnosis age range from birth to 5 years old
- Patient prognosis will be determined by vital status and weeks of survival after diagnosis

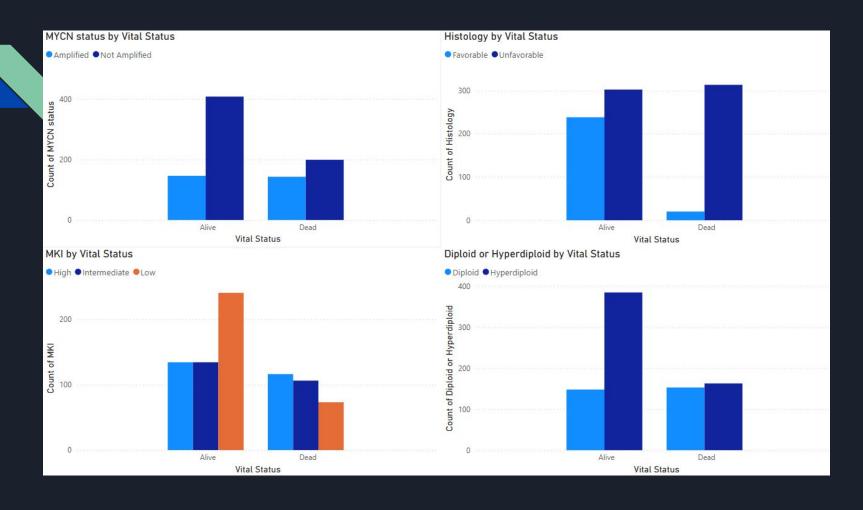






	Survival Time in Weeks							
	mean	std	size					
Gender								
Female	305.542636	192.756592	387					
Male	316.440385	196.454960	520					

	Surv	t-test	p-value			
	mean	std	size			
Diagnosis Age Range in Years						
0-2	347.781863	184.909551	408	3.92	0.00	
10+	295.333333	147.367089	18	-0.47	0.64	
2-5	277.772059	205.290780	408	-3.35	0.00	
5-10	305.319444	165.747035	72	-0.33	0.74	



## Analysis

- Patients w/ diploid chromosome, unfavorable histology and amplified MYCN status have a significantly lower survival time.
- There is a significantly lower survival time between high/intermediate and low MKI
- Patients who survived tended to have a non-amplified MYCN status, a favorable histology, a low MKI status and hyperdiploidy
- No significant variance in sex
- Higher survival time in pt's of diagnosis age range 0-2 years and lower survival time in age range 2-5 years

			Survival Time in Weeks					Survival Time in W			
mean std size								mean	std	size	
	Diploid or Hyperdip	ploid						Histology			
	Dip	ploid	255.4983	339 1	93.87301	0 301		Favorable	400.255814	154.569329	258
	Hyperdip	ploid	347.1697	708 18	36.03979	8 548		Unfavorable	278.089431	198.052621	615
	Unkn	own	269.655	172 2	07.23531	4 58		Unknown	250.088235	200.567735	34
								Sur	vival Time in V	Veeks	
Survival Time in Weeks								mean	std	size	
			mean		std	size		MKI			
	MYCN status							High	279.512000	199.956486	250
	Amplified	253.5	53633	205.4	415377	289		Intermediate	310.162500	198.353734	240
	Not Amplified	338.8	866557	183.6	677757	607		Low	356.383387	178.122455	313
	Unknown	347.7	727273	190.3	315575	11		Unknown	258.932692	196.245253	104

	Male vs Female	MYCN Amplified vs NonAmplified	Diploid vs Hyperdiploid	Histology Unfavorable vs Favorable	MKI High vs Intermediate	MKI Intermediate vs Low	MKI High vs Low
Survival Time t-test	0.84	-6	-6.69	-9.77	-1.7	-2	-4.76
p-value	0.4	0	0	0	0.09	0.046	0
Statistically Significant?	No	Yes	Yes	Yes	No	Yes	Yes

#### Conclusions

- High tumor break load indicates reduced survival time in patients w/ adrenocortical carcinoma
- A lower aneuploidy score and percent genome altered is associated with paragangliomas, which tend to be more dangerous than pheochromocytoma
- Diploidy, unfavorable histology, amplified MYCN status and high and intermediate MKI indicate a reduced survival time in patients with neuroblastoma
- Higher survival time in neuroblastoma pt's diagnosed from birth to 2 years of age, and lower survival time for pt's diagnosed from 2-5 years old
- Most conclusions are made using samples with a White majority and a relatively even gender distribution

#### References

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