

Prevalence of somatic *SF3B1* mutation in lactotroph tumours

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Background

- *SF3B1* mutations are common in human cancers, but rarely reported in pituitary tumours
- Whole exome sequencing in 27 lactotroph tumours detected pathogenic *SF3B1* mutations in ~20% of cases¹

Aim of the study

Determine the prevalence of *SF3B1* mutations in a non-Asiatic cohort of lactotroph tumours

Results

SF3B1 mutations are rare in a European multicentre cohort

- *SF3B1* c.1874G>A (p.Arg625His), heterozygous, likely pathogenic
- Found in 4/101 (3.96%)
- Found in 2/3 carcinomas
- No clinical control achieved (Fisher's exact test P=0.004)

Table 2. Clinical characteristics of patients with *SF3B1* mutant tumours

#	Sex	Age at diagnosis	Diagnosis	Basal PRL (µg/L)	DA therapy response	# total surgeries	Radiation	TMZ	Other therapy	Survival
1	M	54	Lactotroph carcinoma	4784	No	4	yes	yes	Cisplatin/Etoposid Pasireotid, Pembrolizumab	No
2	M	58	Lactotroph carcinoma	NA	No	3	yes	yes	Temodal/ Bevacizumab	Yes
3	M	27	Lactotroph Macroadenoma	6511	NA	1	yes	NA	Cabergoline	Yes
4	M	17	Lactotroph macroadenoma	950.1	Partial	1	no	no	-	Yes

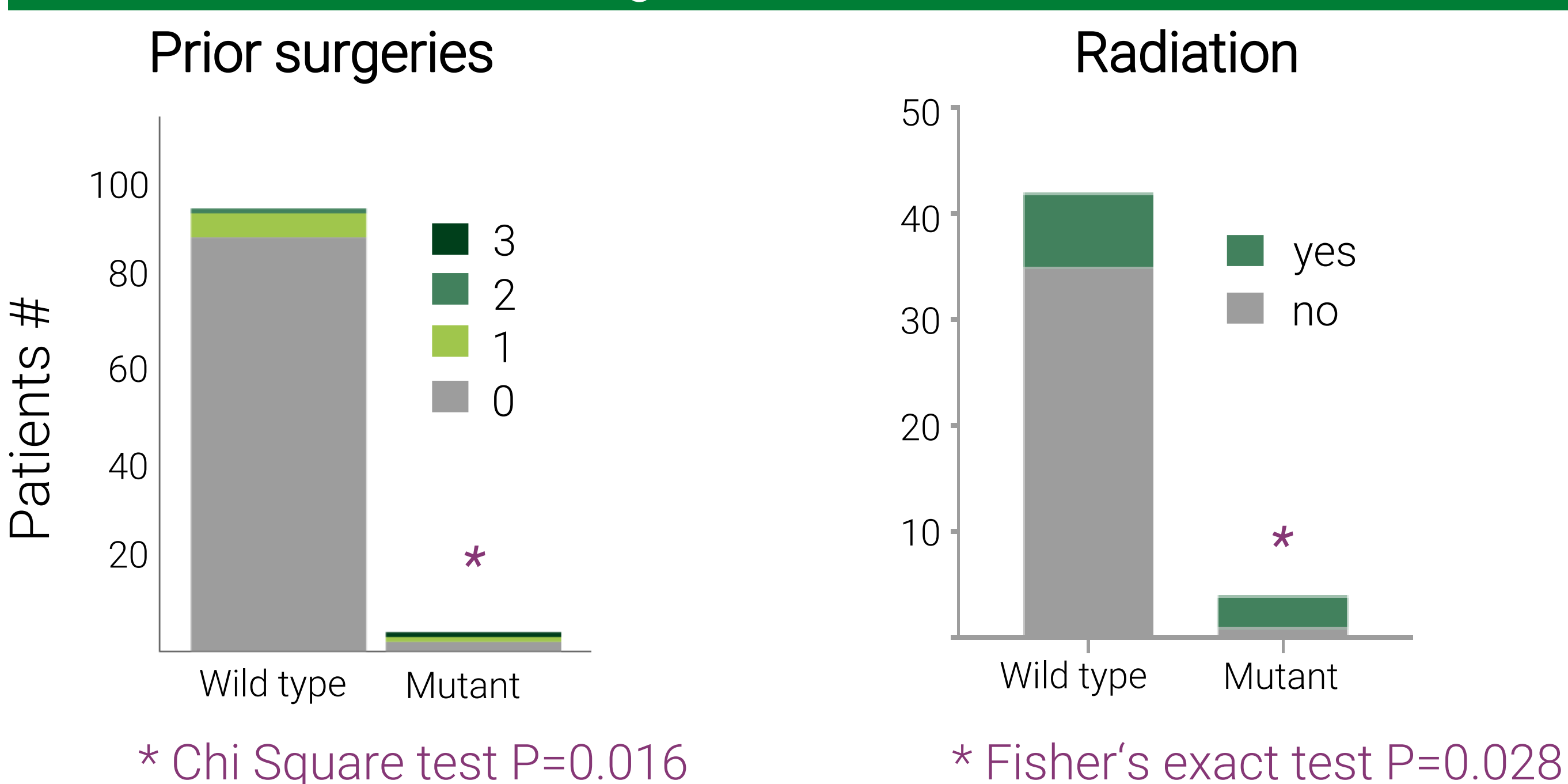
Patients and Methods

- Multicentre:
 - 98 lactotroph tumours (54M, 44F)
 - 3 lactotroph carcinomas (3M)
 - Mean age at surgery: 42±14 (17-72) years
 - Mean follow up time: 112±82 (0-401) months
- Fresh-frozen (DNA extraction: Maxwell)
- PCR amplification of *SF3B1* hotspot R625 region
- Sanger Sequencing; Mutation Surveyor, Ensembl GRCh38.p13

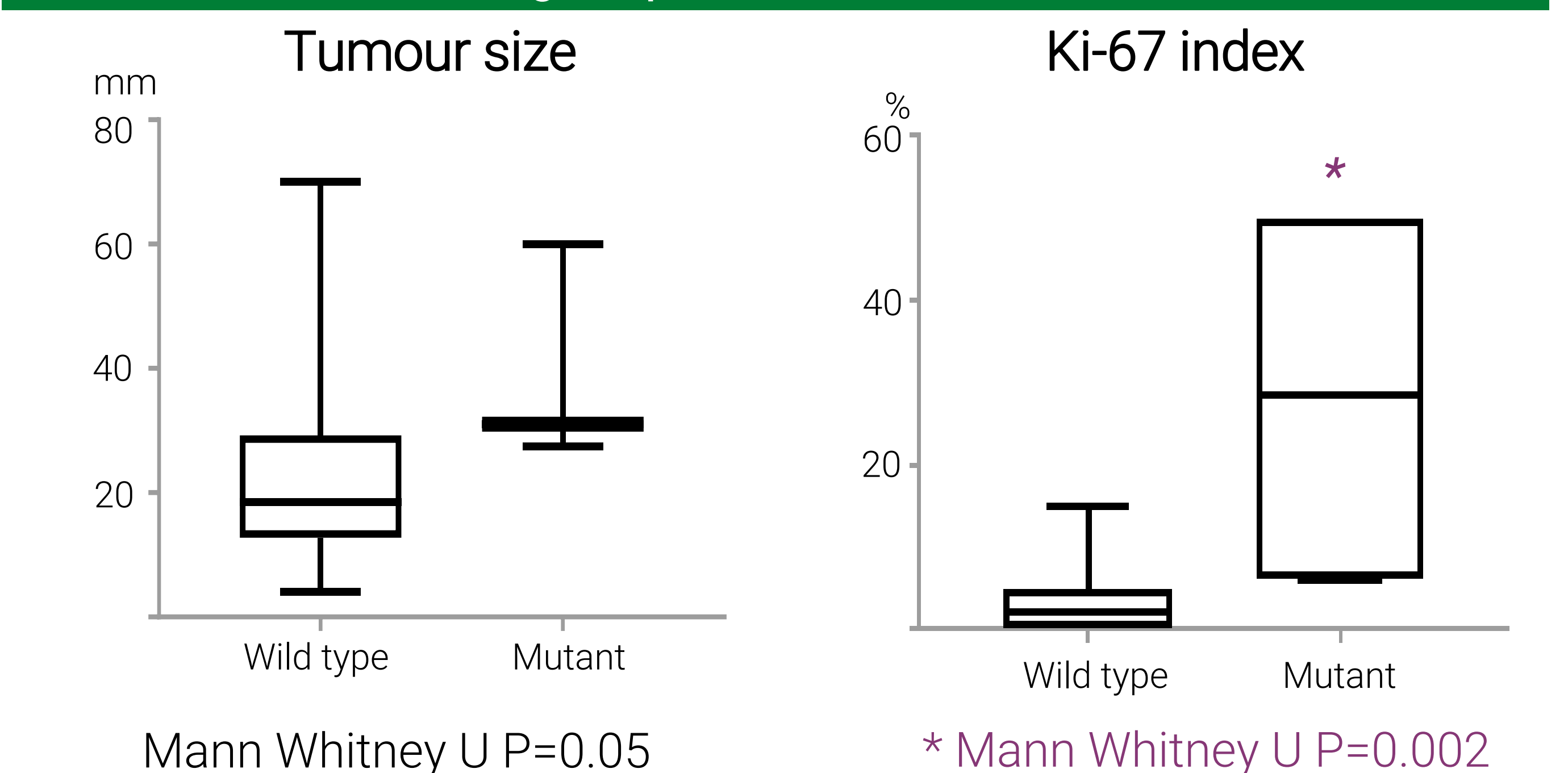
Table 1. *SF3B1* mutant tumour characteristics

#	sample	Tumour size (mm)	Invasion	Ki-67 index (%)	Total resection
1	Metastasis	-	-	50	
2	Primary tumour	27.5	yes	50	No
3	Primary tumour	60	yes	6	No
4	Primary tumour	31	yes	7	No

Patients with *SF3B1* mutant lactotroph tumours have more prior surgeries & radiation



SF3B1 mutant tumours tend to be bigger and have significantly higher proliferation index



Conclusion

- *SF3B1* c.1874G>A (p.Arg625His) variant is uncommon in lactotroph tumours (< 4% in European cohort)
- Is linked to aggressive lactotroph tumours and carcinoma

References

1 Li et al., 2020, Nature Communications