Molecular characterisation of lung neuroendocrine tumours through innovative technologies

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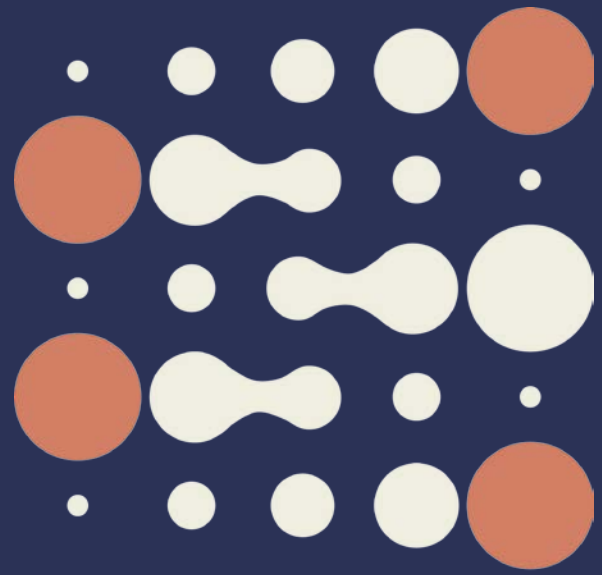


International Agency for Research on Cancer

World Health Organization

RARE CANCERS GENOMICS

www.rarecancersgenomics.com

Introduction

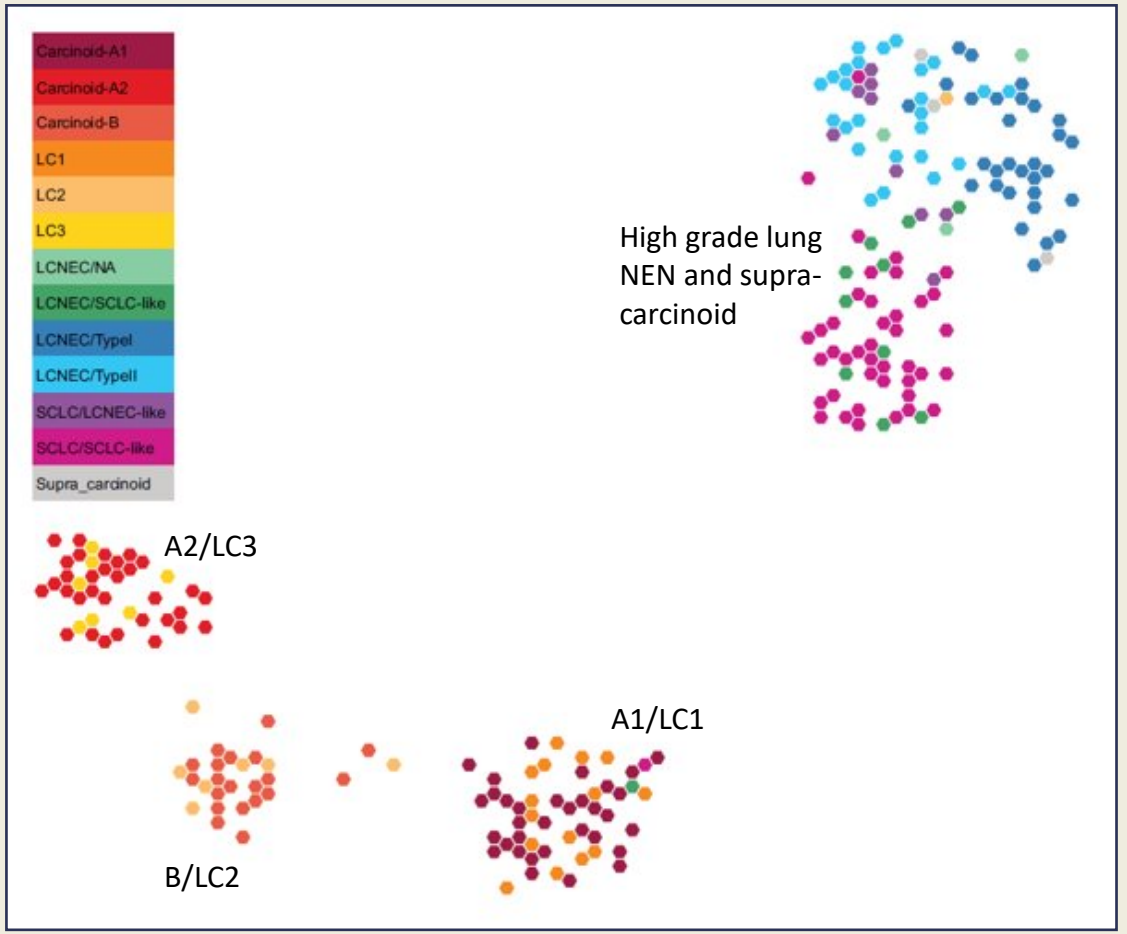
	Atypical pulmonary carcinoid	Typical pulmonary carcinoid
WHO grade	G2	G1
Epidemiology	Female 50s	Female 50s
Necrosis	Focal, if any	No
Mitosis per 2mm²	2–10	<2
10-year OS	51% (38–74)	89% (60–100)

Lung neuroendocrine Tumours (LNETs)

DATA NOTE

A molecular map of lung neuroendocrine neoplasms

Aurélie AG Gabriel[1,†], Emilie Mathian[1,†], Lise Mangiante[1], Catherine Voegele[1], Vincent Cahais[2], Akram Ghantous[2], James D. McKay[1], Nicolas Alcala[1], Lynnette Fernandez-Cuesta[1,‡] and Matthieu Foll[1,*,‡]



WHO Classification of Thoracic Tumours, 5th edition, vol. 5, 2021; Dingemans A-M.C *et al*. Annals of Oncology, 32(7), 2021; Derks JL *et al*. Journal of Thoracic Oncology, 16(10), 2021. Gabriel AAG *et al. GigaScience,* 9(11), 2020.

Design

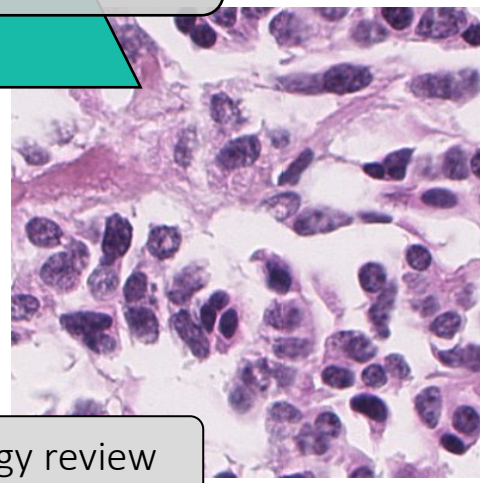
lungNENomics

Unveiling the molecular pathways underlying the development of lung neuroendocrine neoplasms

WGS sequencing

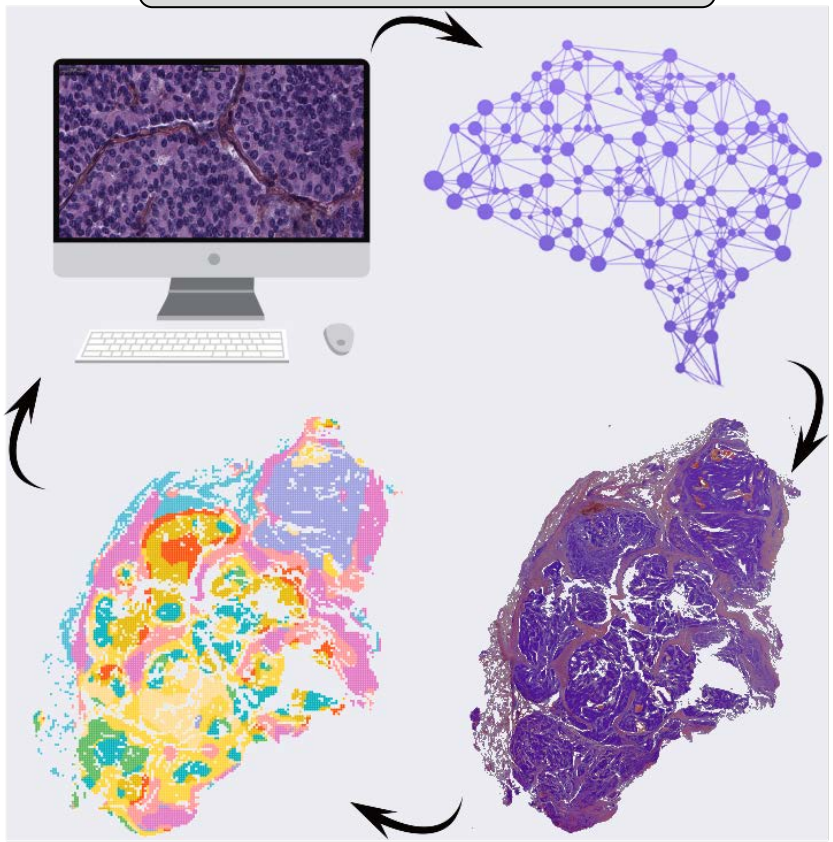
RNA sequencing

DNA methylation array

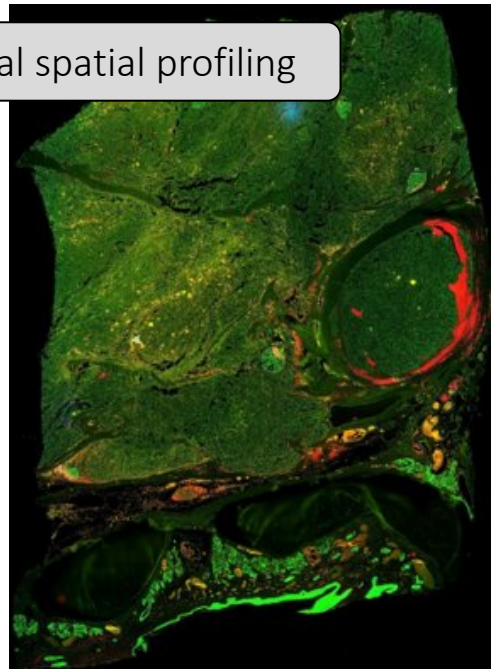


Central pathology review

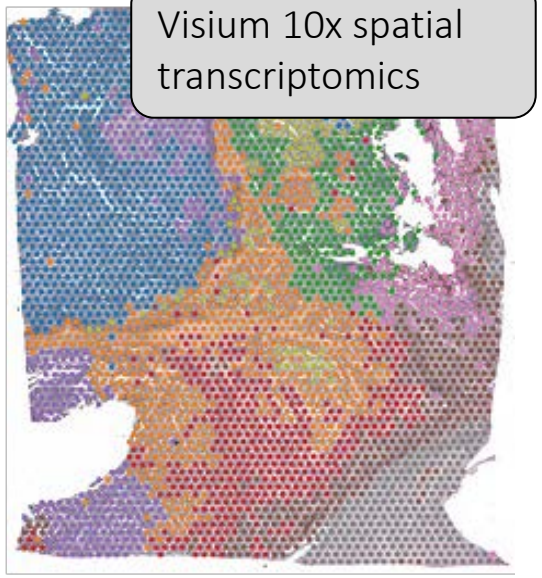
Deep-learning image analysis



Digital spatial profiling

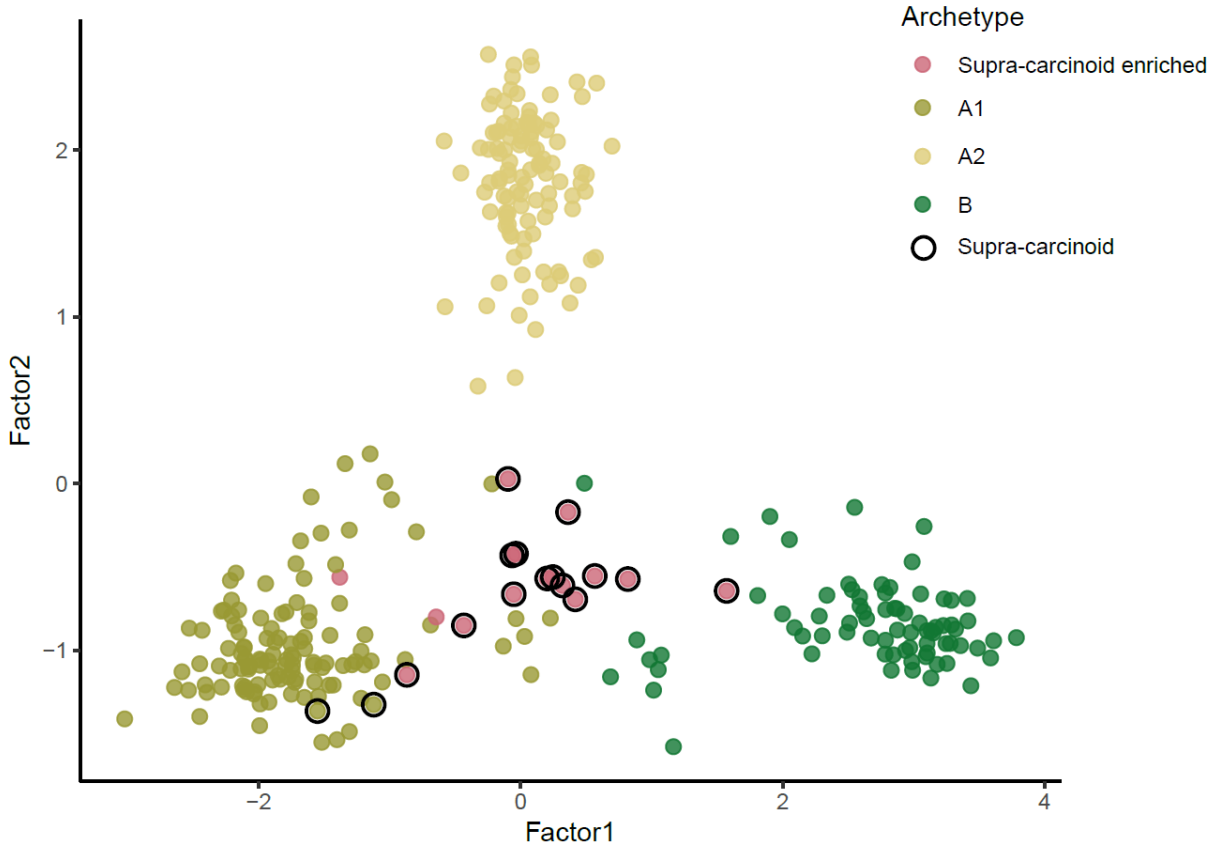


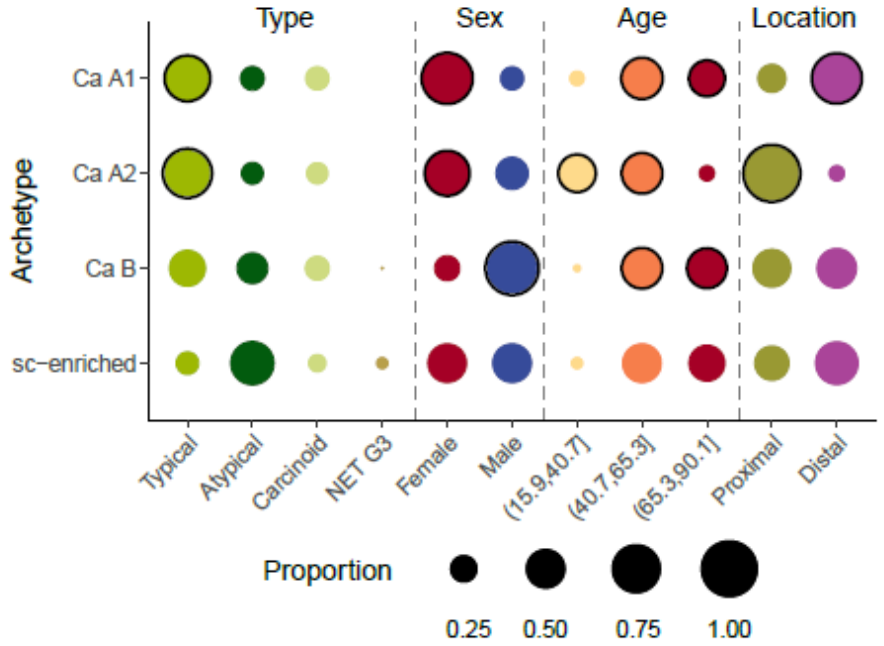
Visium 10x spatial transcriptomics

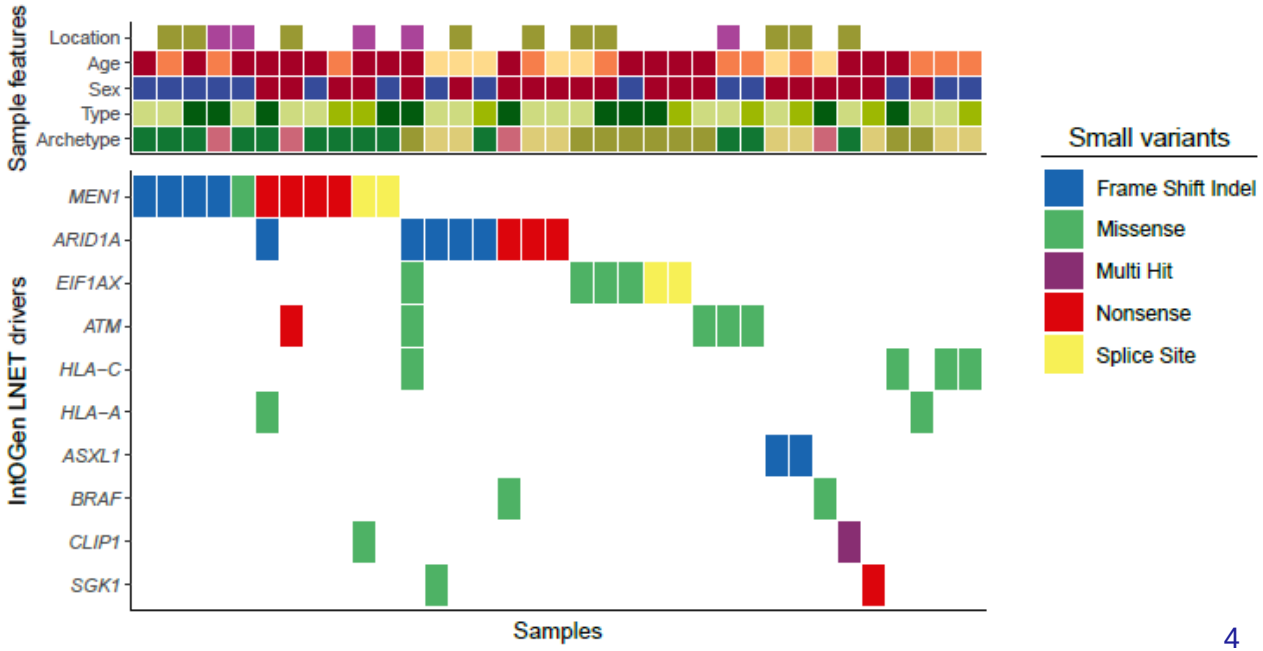


Results: Identification of molecular groups with distinct epidemiological and genomic features

Sexton-Oates A, Mathian E, *et al.* In preparation.

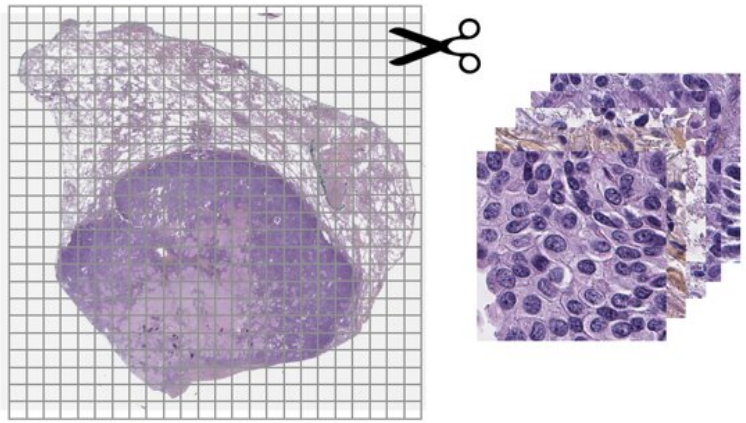


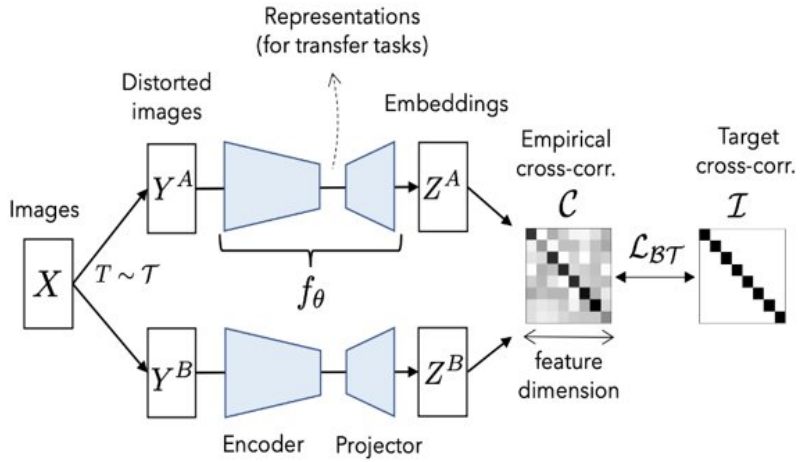


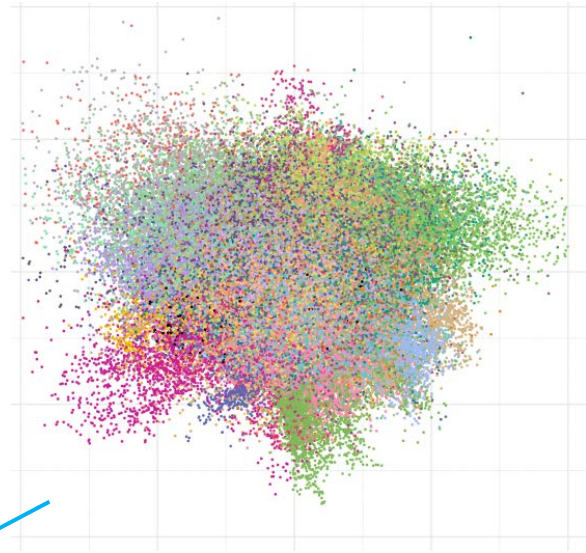


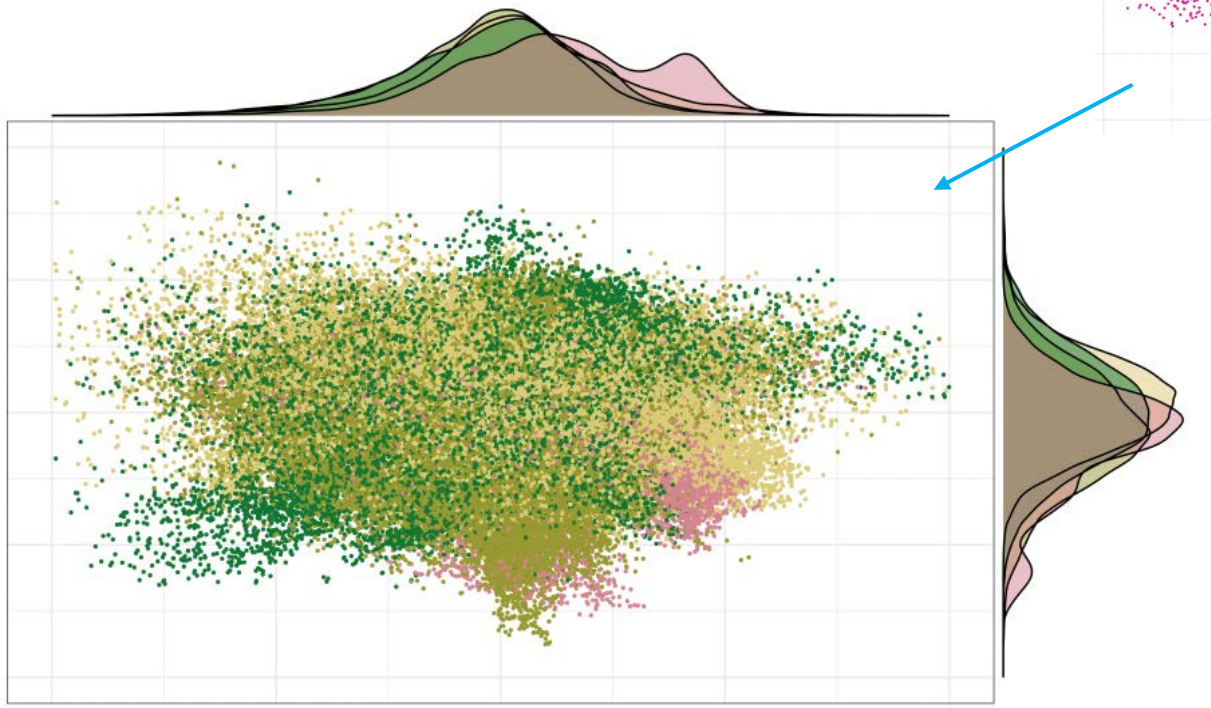
Results: Deep-learning image analysis better identifies distinct morphological communities between molecular groups than between tumour types

Mathian E, *et al.* Under Review



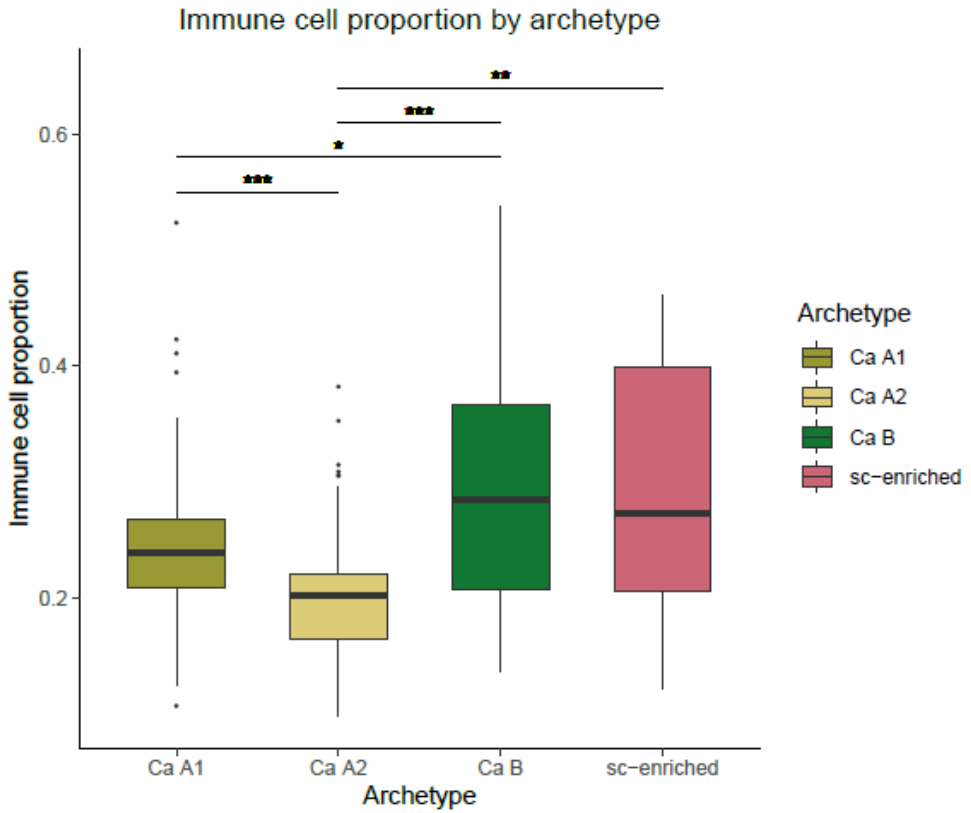


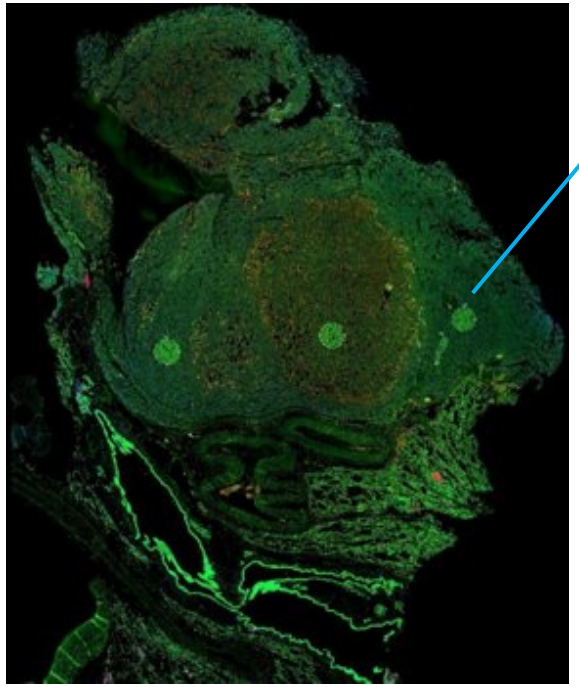


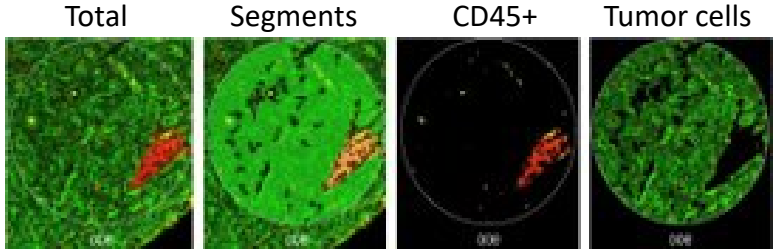


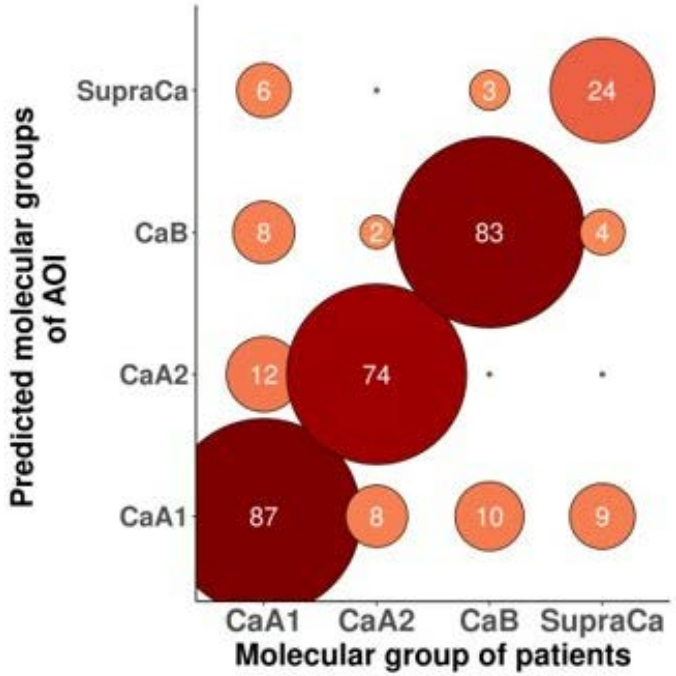
Results: Immune micro-environment is variable between molecular groups, and particularly heterogeneous in supra-carcinoids

Sexton-Oates A, Mathian E, *et al.* In preparation.







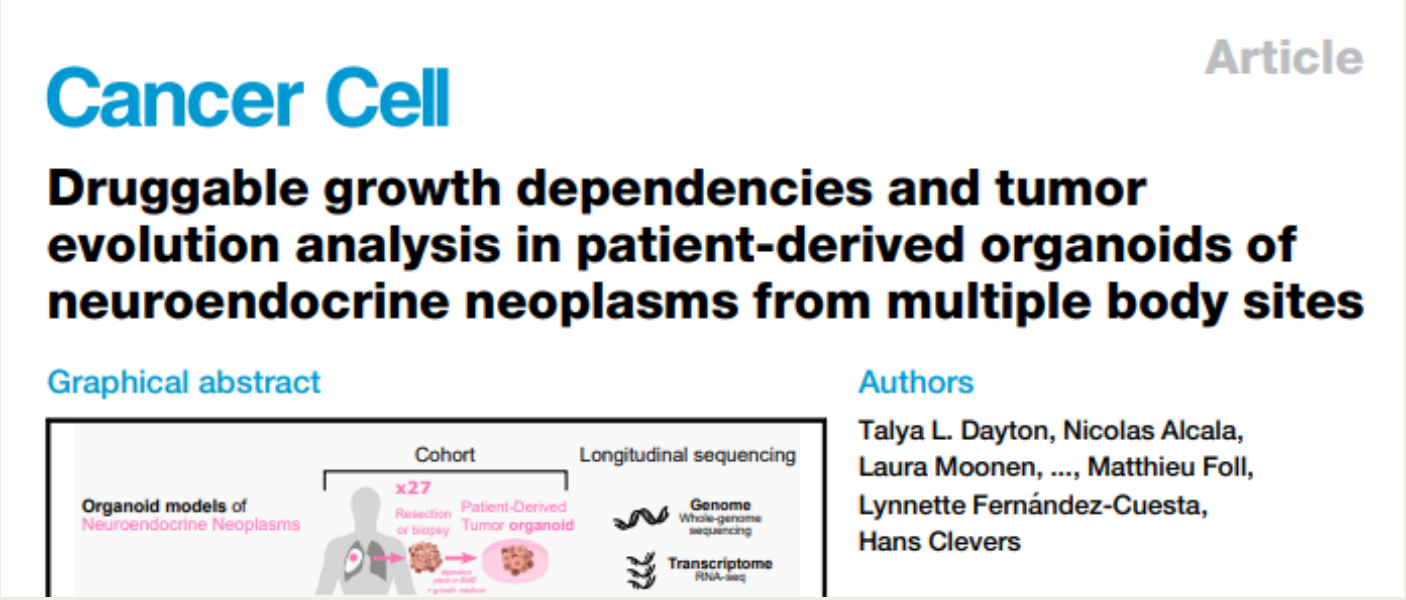


Discussion and Conclusions

Existence of four molecular groups of lung neuroendocrine tumours with variable:

- Epidemiology
- Genetics
- Morphology
- Immune micro-environment

New model systems can teach us more about their development



Potential to impact public health through improving classification systems, intercepting tumours at an early stage, and putting patients on the right path for personalised cancer management

Key take-home messages

Integration of multi-omic and spatial data analysed with cancer evolution approaches, coupled with whole-image deep learning analyses, provides a comprehensive molecular and morphological understanding of lung neuroendocrine tumours.