Tumor and stroma cell content of human pancreatic ductal adenocarcinoma

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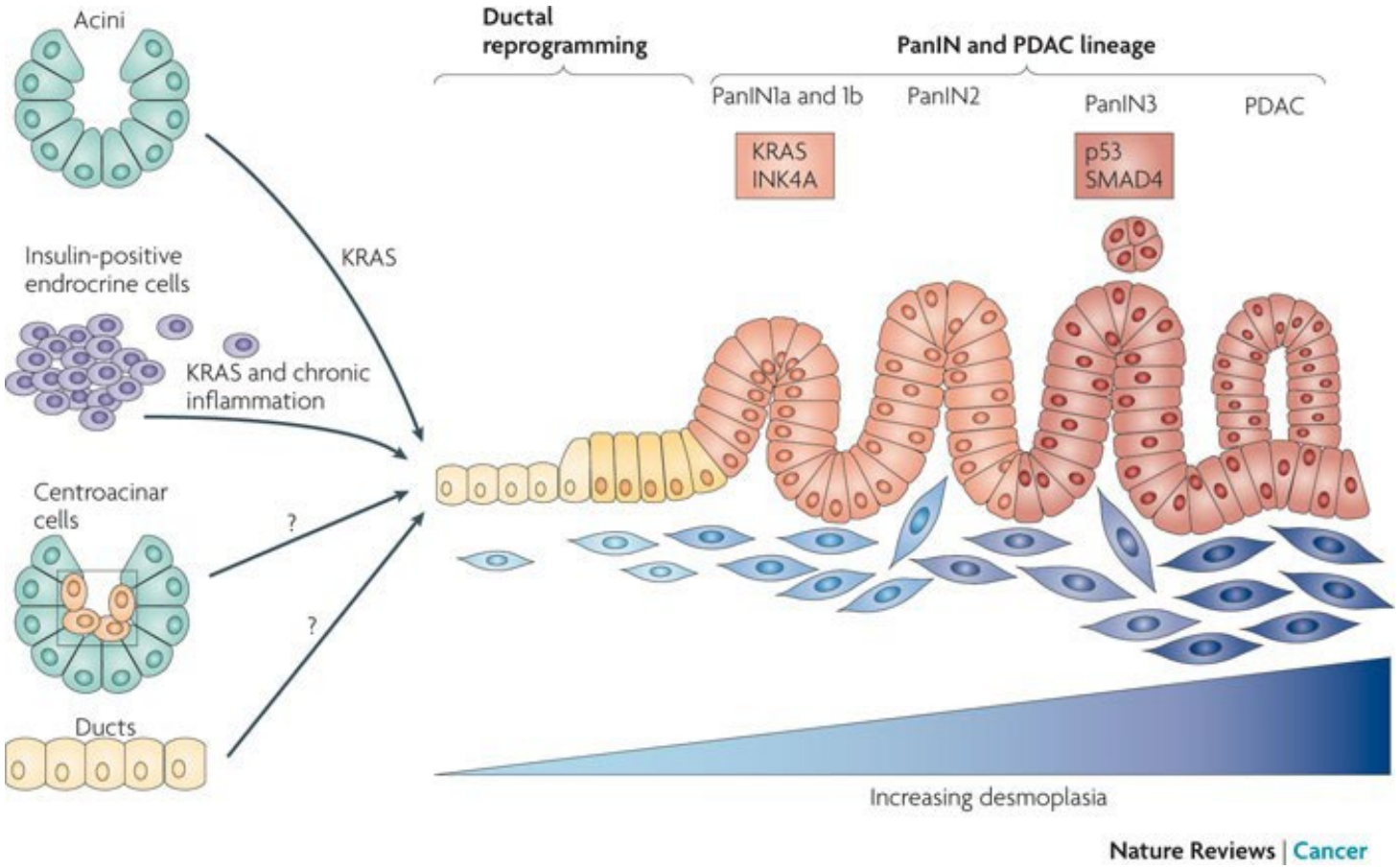
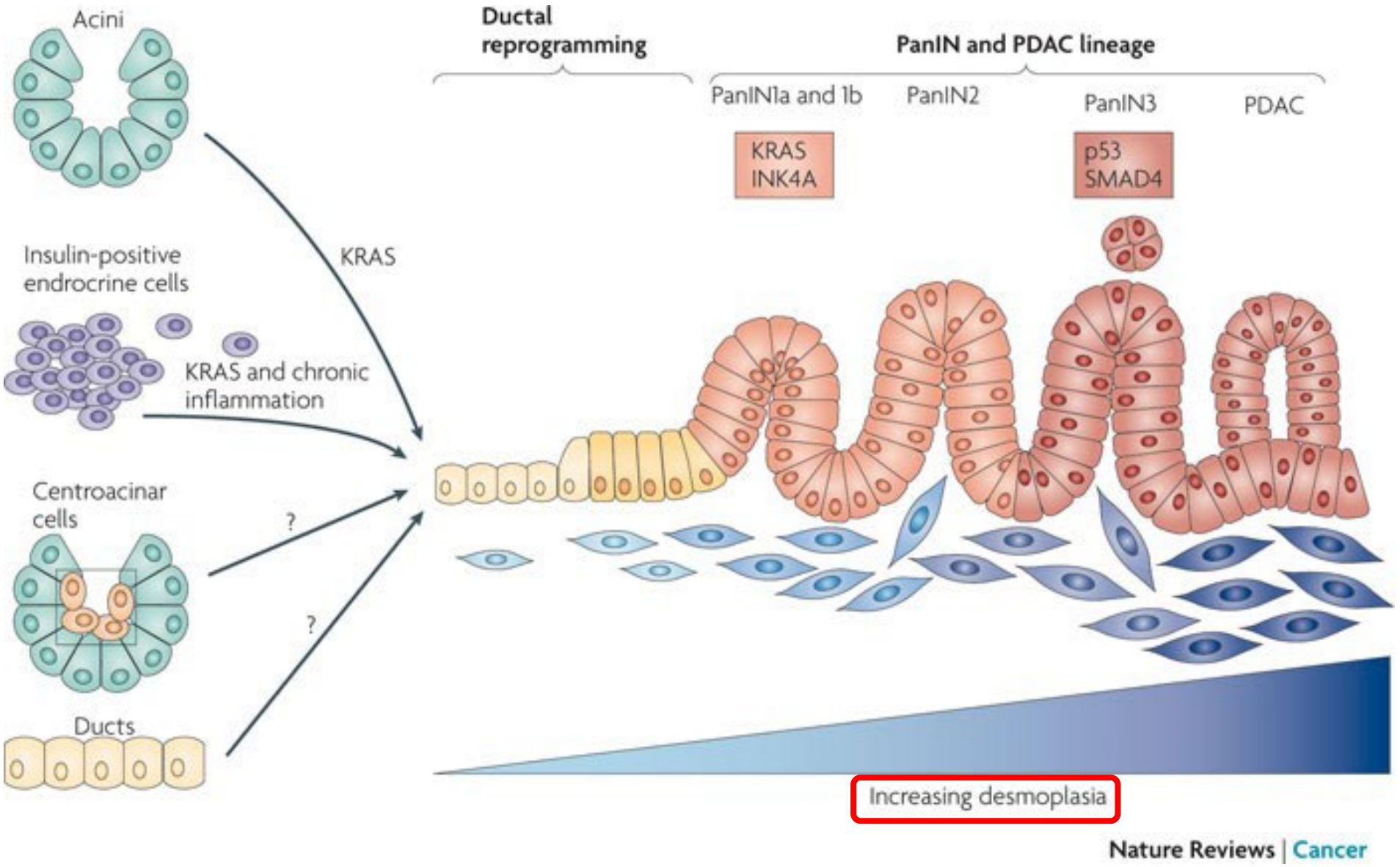
Pancreatic Ductal Adenocarcinoma (PDAC)

- Most common type of pancreatic cancer
- Low survival rate
- Primary tumors develop asymptomatically overtime
- Diagnosis and symptomatic at point of treatment-resistant distant metastasis
- Primary tumors are surrounded by a “desmoplatic”, dense, fibrotic, nutrient-poor stroma.



Morris, J., Wang, S. & Hebrok, M. KRAS, Hedgehog, Wnt and the twisted developmental biology of pancreatic ductal adenocarcinoma. Nat Rev Cancer **10**, 683–695 (2010). https://doi.org/10.1038/nrc2899



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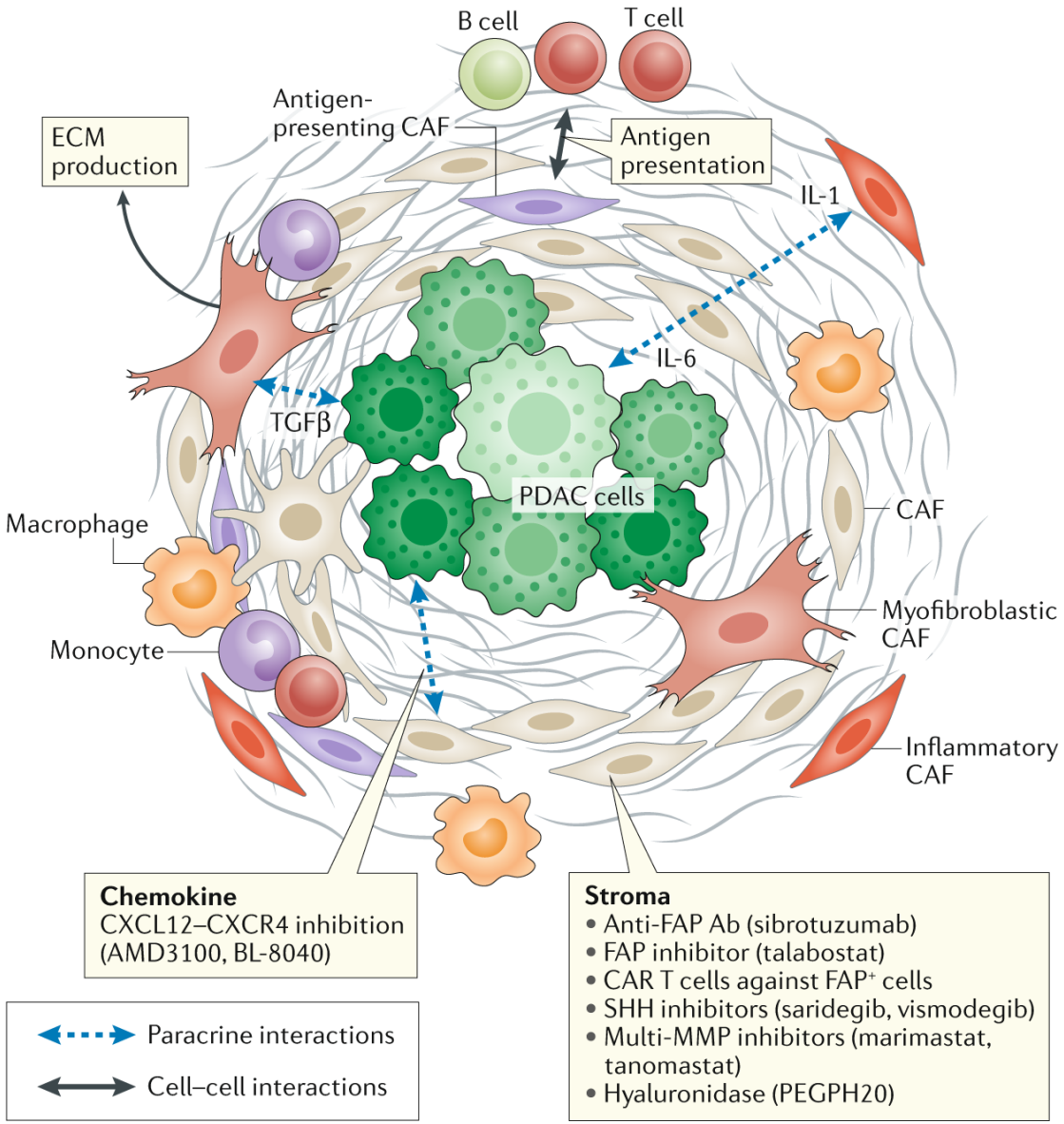
PDAC Tumor Microenvironment (TME)



- "Desmoplastic" stroma (CAFs, ECM, immune cells)
- CAFs are diverse: iCAF, myCAF, transitional
- Immunosuppressive immune cells: Tregs, TAMS
- CAF:Immune cell interactions are known to govern tumor immunity
- **Little is known about the differences between primary metastatic PDAC TMEs**

Ho, W.J., Jaffee, E.M. & Zheng, L. The tumour microenvironment in pancreatic cancer — clinical challenges and opportunities. *Nat Rev Clin Oncol* **17**, 527–540 (2020). https://doi.org/10.1038/s41571-020-0363-5

Single cell RNA-Sequencing data sets

- One set of matched primary (n=8)/peritoneal(n=4)/distant metastases(n=7) from HTAN
- All unsupervised algorithms: Iteratively harmony normalized, find neighbors, find clusters, cleaned.

PDAC Patient Histopathology Samples

- PDAC cases retrieved at our institution (n=401 biopsies, 272/401 untreated; n=308 patients)
- Included primary tumors (n=155), liver metastases (n=180), peritoneal implants (n=41), lung metastases (n=20), and bone metastases (n=5).

Goals for IDSC Fellowship

- Single Cell RNA Seq
  - Increase sample size
- Machine Learning
  - Use 400+ digitalized pathology H&E Slides to write a machine learning algorithms that will
    - Orthogonally score pathology specimens (Growth, Activity, Cytology, Stroma)
    - Derive approaches to quantitate Stromal Cell infiltration