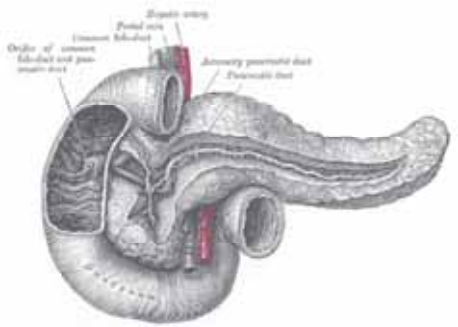


Pancreatic Stem Cells: An *In-Vitro* Study

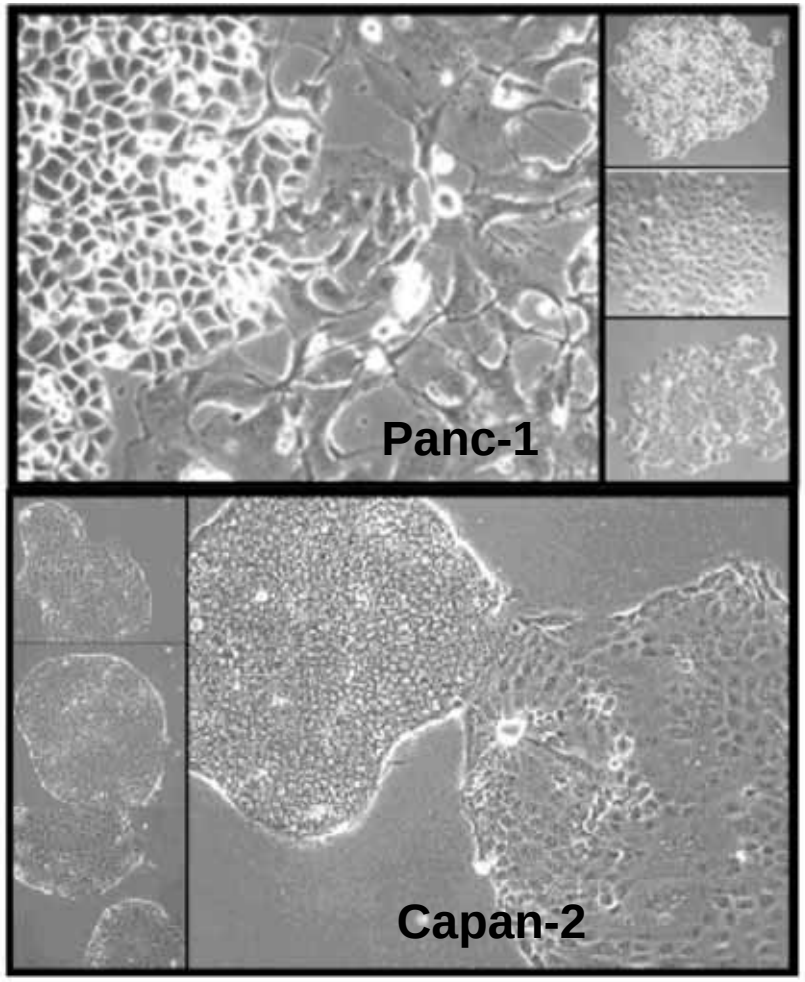
Miss N J Guppy
Institute of Cellular and Molecular Science
QMUL, London, UK

Why pancreatic stem cells?

- Pancreatic cancer is the 5th commonest cause of cancer death in the UK, with the lowest survival rate of any cancer
- 3 million cases of diabetes in the UK by 2010
- A cancer stem cell represents an attractive therapeutic target as the unique tumour cell type from which new and recurring tumours originate
- An adult tissue-based stem cell is an attractive target for manipulation for β-cell replacement in diabetes
- No definitive stem cell

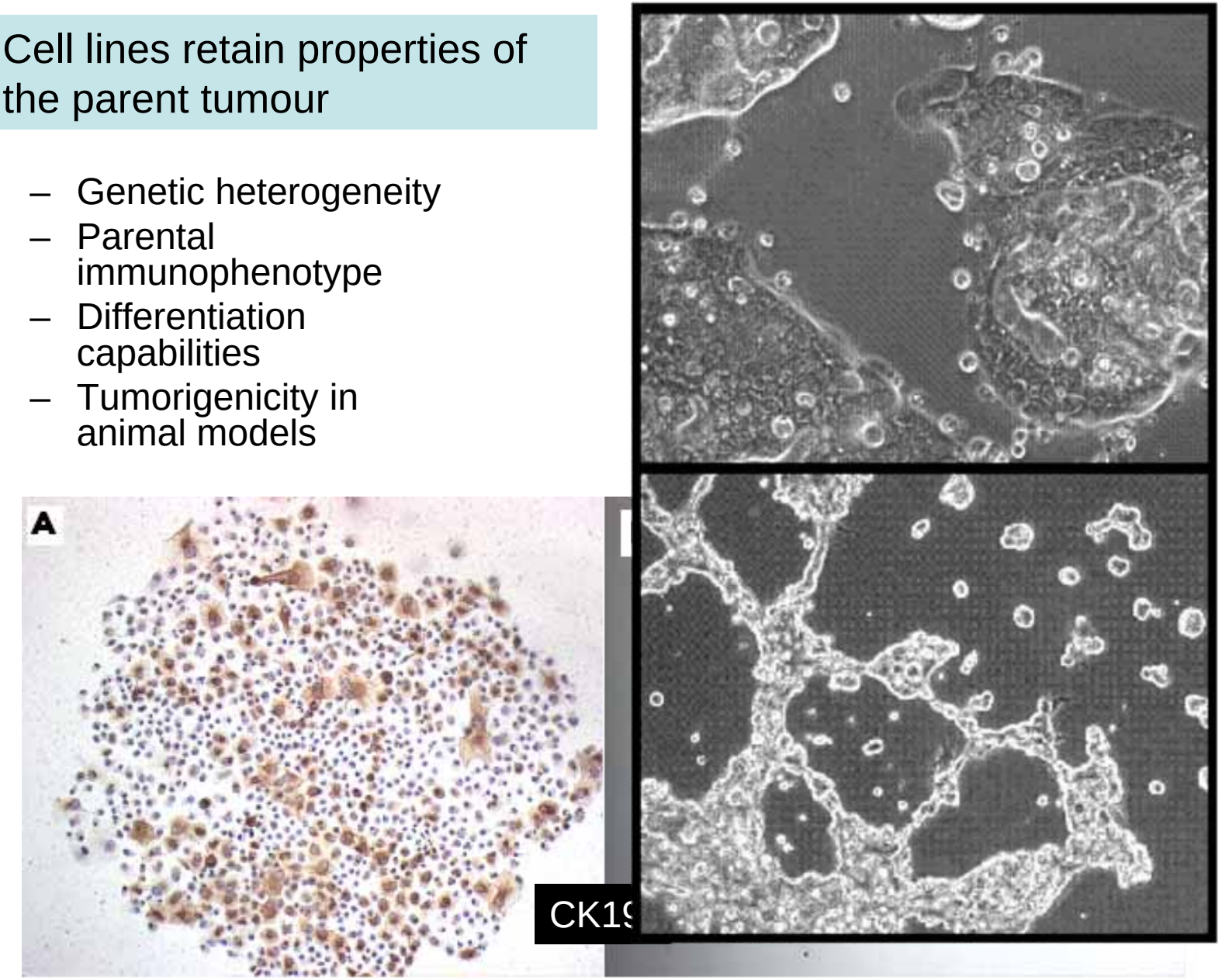
An *in vitro* study…

- Human material
  - Cell lines (Panc-1, Capan-2) are readily available
  - Primary tumour explants
- Can investigate one attribute at a time in an easily manipulated environment



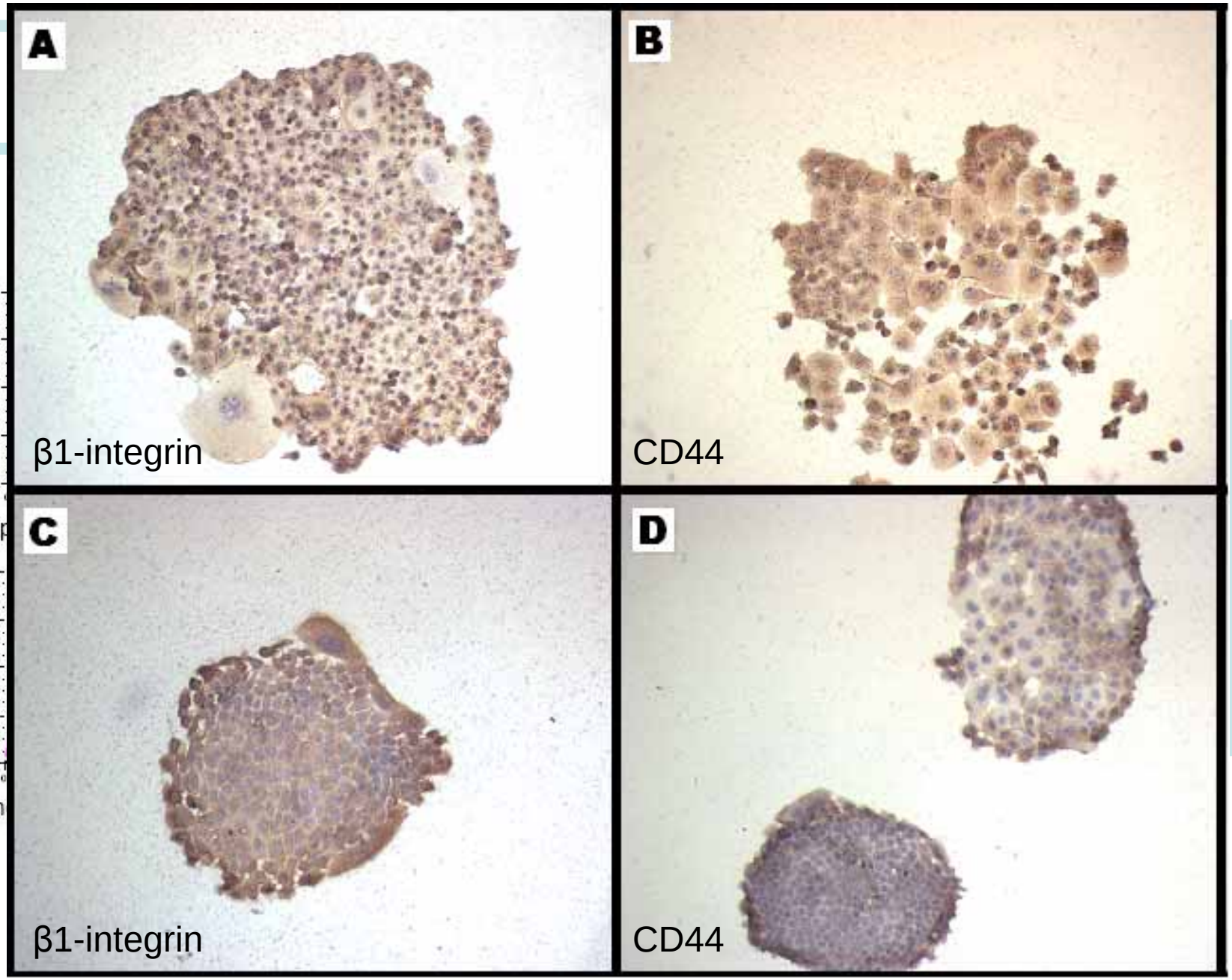
Cell lines retain properties of the parent tumour

- Genetic heterogeneity
- Parental immunophenotype
- Differentiation capabilities
- Tumorigenicity in animal models



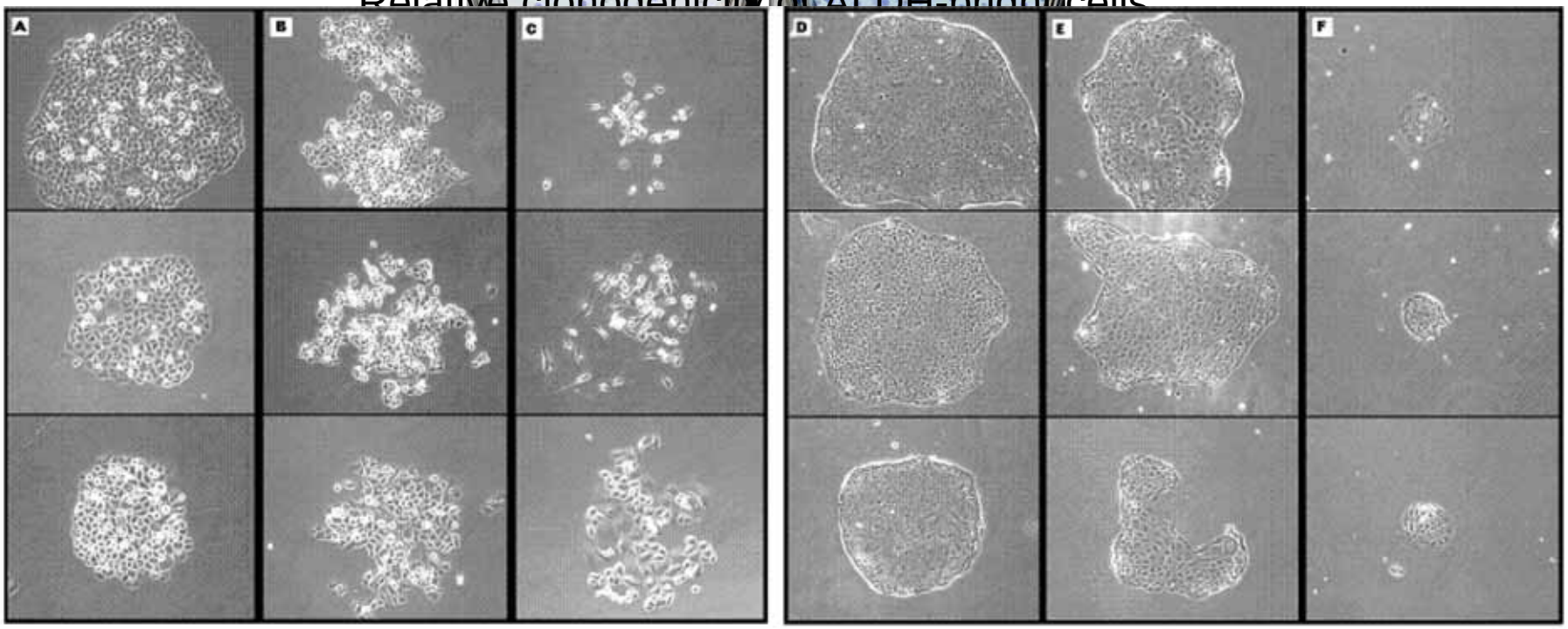
Caveats and disadvantages…

- Genetic heterogeneity
  - Culture adaptation
- Simplistic artificial environment
  - Extra-cellular matrix
  - Interactions with tumour stromal cells
  - Systemic factors
  - Careful selection of media
- **Does *in vitro* behaviour truly reflect *in vivo* function?**


A
β1-integrin
B
CD44
C
β1-integrin
D
CD44

Investigat ll Kinetics

Relative clonogenicity of ALDH-bright cells



Heterogeneous clone morphologies

** p<0.005 student's 2-tailed t-test

negative positive

CD133

SUMMARY

Preliminary Results

1. ALDH-bright and SP sub-populations exist in both lines
2. Heterogeneous morphologic colony types exist in both lines
3. Expression of putative stem cell markers CD133, CD44 and β1-integrin is seen in both lines
4. Significantly increased clonogenicity is seen in Panc-1 ALDH-bright and CD133+ cells compared to controls

Further Work

Stem Cell Kinetics

- Label retention
  - Relative quiescence
  - “Immortal strand”
- Asymmetric division
  - Fate of progeny

- Motility (migration assay)
- Invasive potential (transwell assay)
- Interactions with stromal cells
  - Pancreatic stellate cells: desmoplasia
  - Paracrine and contact-mediated effects
  - Signalling pathways e.g. Notch, Shh
- Adhesive properties
- Immunophenotype
- Differentiation potential/plasticity

THE ACID TEST…

Do these cells function as stem cells

in vivo?

Discussion Points

- Can *in vitro* explorations of cell characteristics (e.g. stem cell function) replace *in vivo* explorations of tumorigenic potential?

- Are there robust, comprehensive studies correlating *in vitro* characteristics to *in vivo* functions?
  - If not, would this be a valuable exercise?
  - If so, could these be made freely available to new researchers?

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