

Keloid Fibroblast Heterogeneity and the Development of an Anti-Recurrence Keloid Biomaterial Treatment



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Keloid scars

- Occur during wound healing
- Scar tissue outgrows original wound boundary
- Risk differs across populations

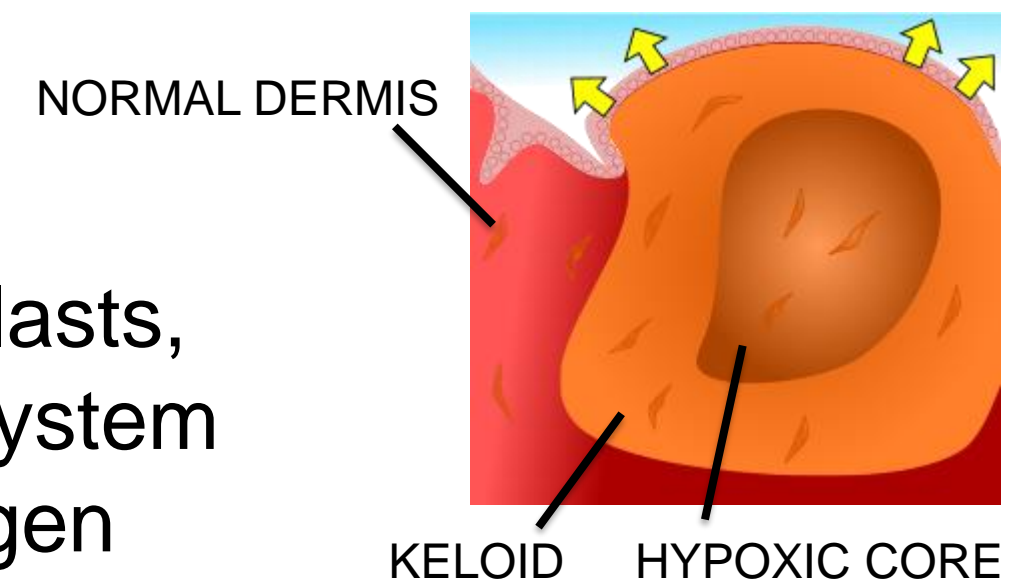


Keloid treatment

- Notoriously hard to cure
- Surgical excision, radio-;chemo-;cryotherapy drug treatments, dressings
- Recurrent growth often worse than original

Keloid pathology

- Much still unknown
- Involves aberrant fibroblasts, other cell types, immune system
- Overproduction of collagen



AIM: DEVELOP A KELOID FIBROBLAST-INHIBITING DERMAL SCAFFOLD

Proposed Treatment Method

- Surgical incision allows application of a dermal scaffold, 2 benefits:
 - 1) Management of wound healing – i.e. tension, shape
 - 2) Specific anti-cell activity
- Can still use adjunct treatment

Scaffold design criteria

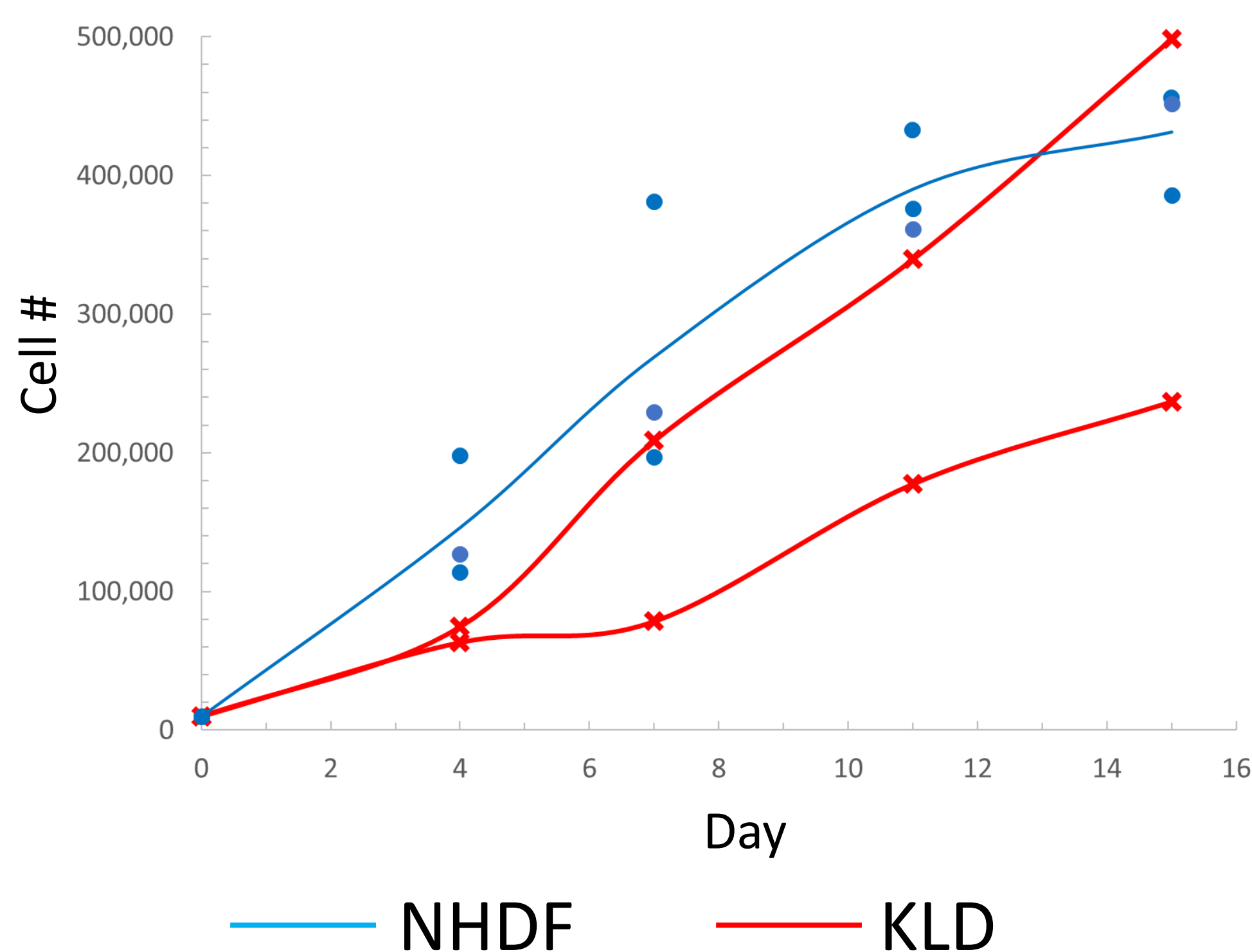
- Minimal inflammation
- Usability consistent with current scaffolds
- Tailored persistence in wound / resorption
- Biological activity: distinguish pathological fibroblasts from normal

RAFT cell bank

- Fibroblasts derived from keloid biopsy 1996-2003 (n=30)
- Cells recovered, expanded and characterised (n=12, process ongoing)

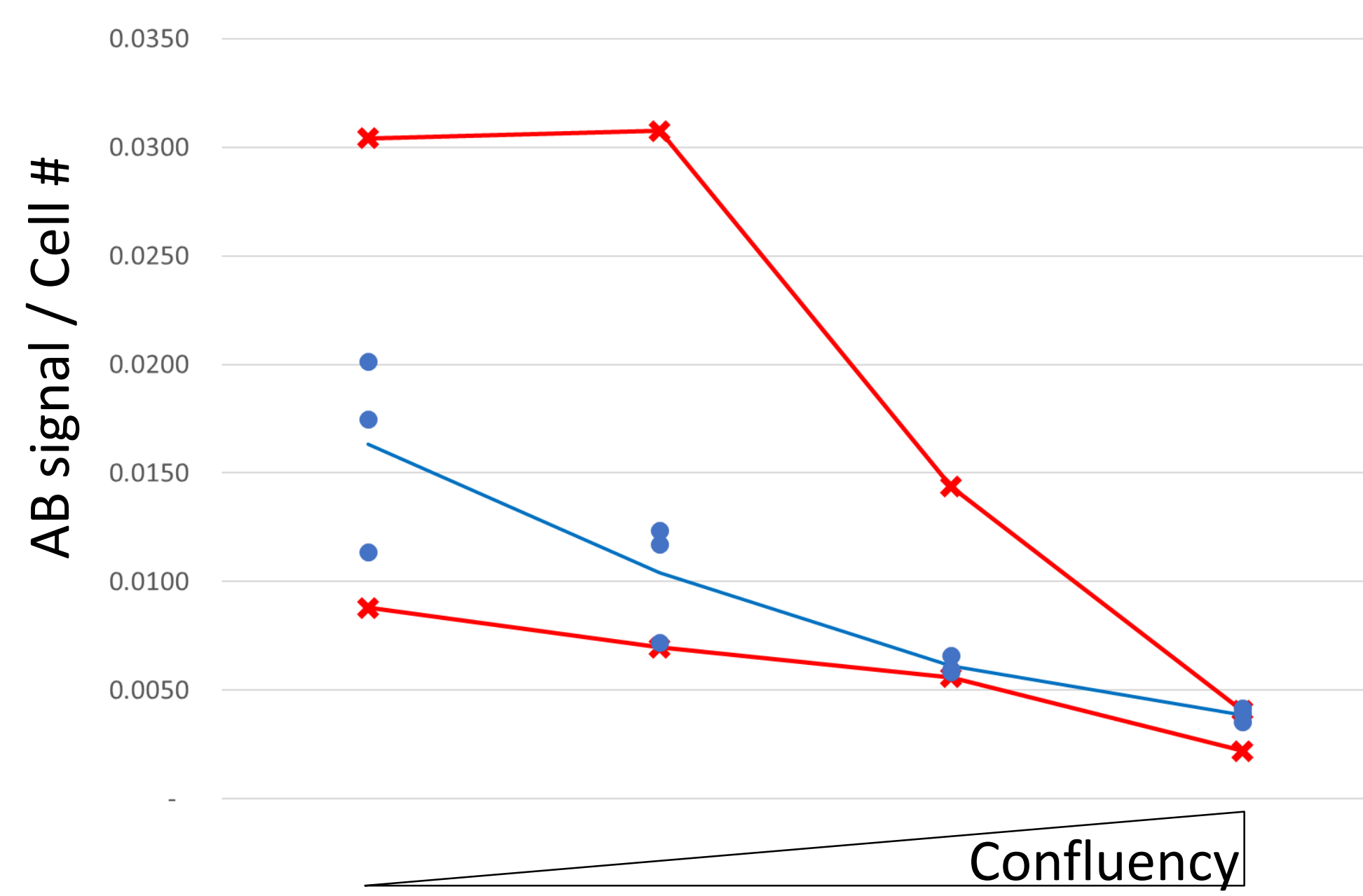
Proliferation of keloid cells

- kFBs reported as more proliferative, with lower serum requirement than normal fibroblasts¹
- kFBs highly variable, some lines more proliferative, some not



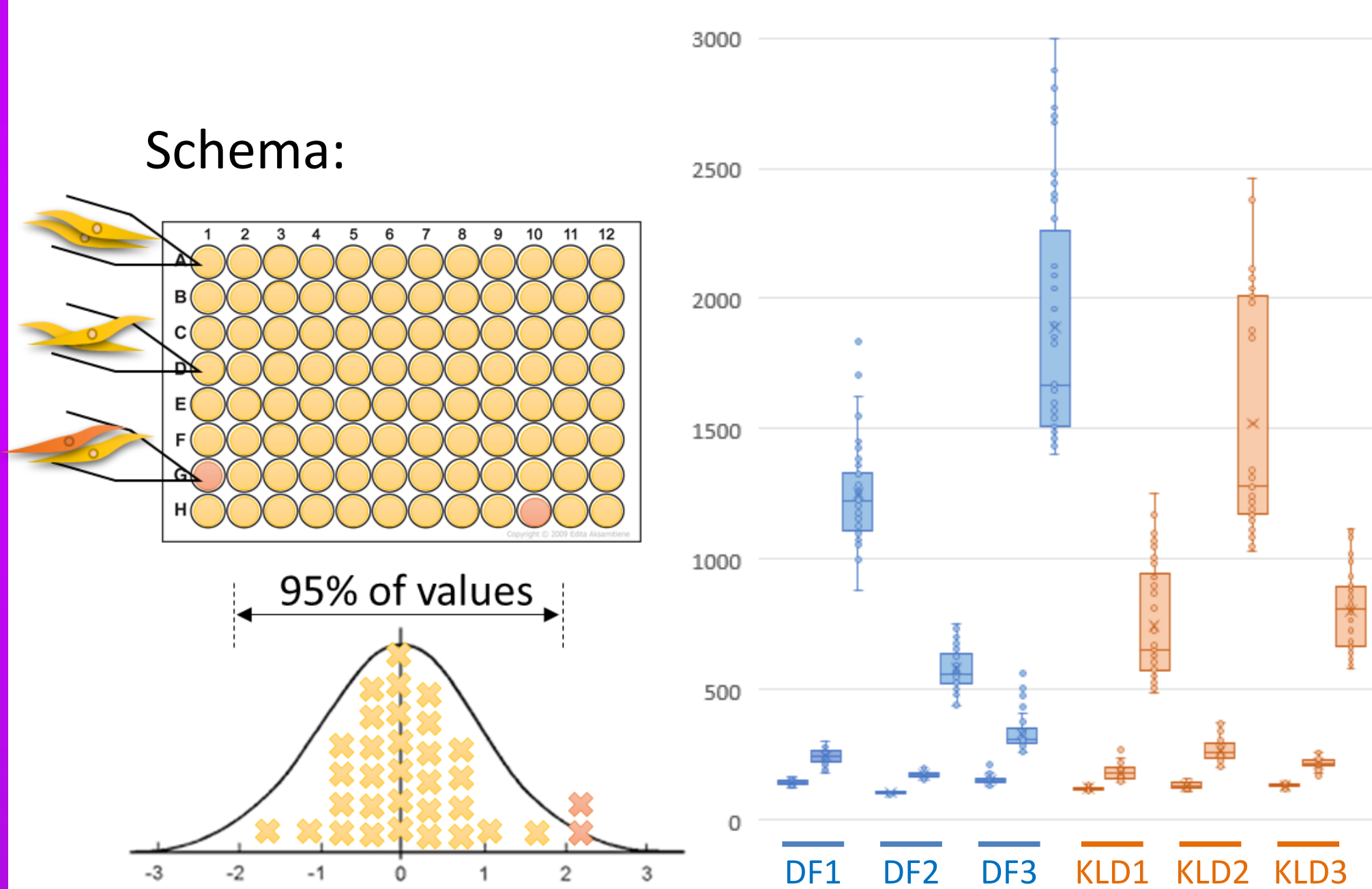
Metabolic rate of keloid cells

- kFBs reported as more metabolically active than normal fibroblasts²
- kFBs and controls given AlamarBlue reagent ("AB", 2hrs), measure fluorescent change as substrate metabolised.
- Highly active kFB still show contact inhibition



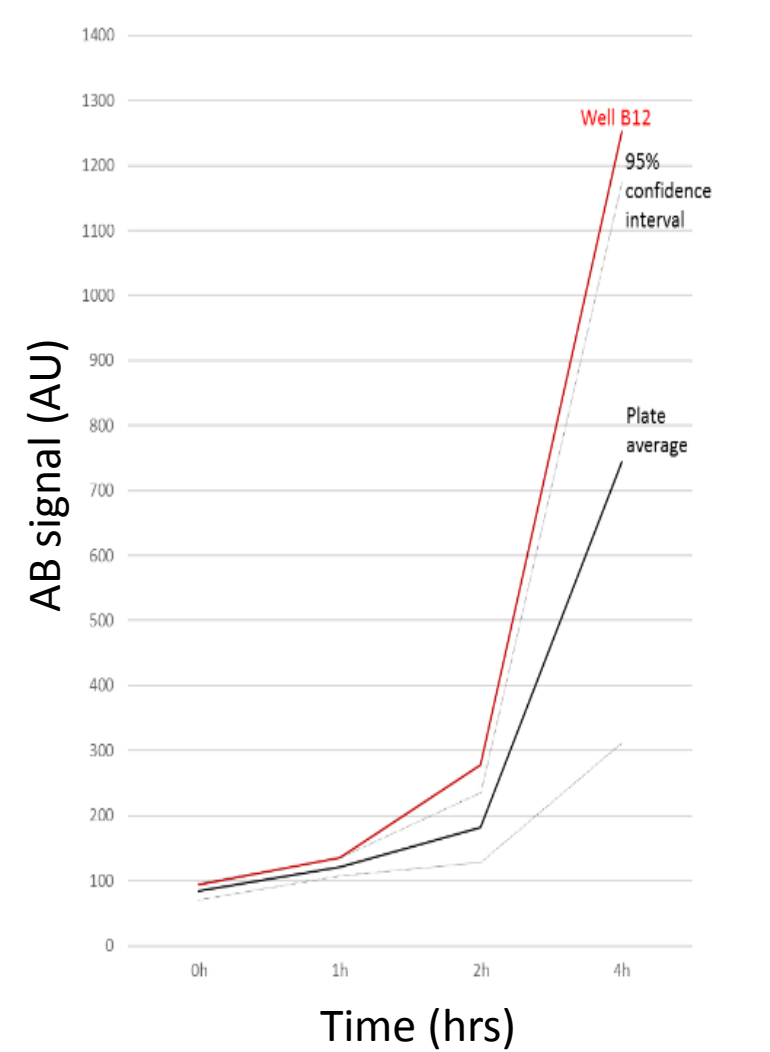
Heterogeneity present in keloid fibroblast isolates

- In vivo, keloid tumours show heterogeneity³: in kFB culture?
- Seed kFBs at low density on 96 well plate (5000 cells / well)
- Follow AB metabolism
- Heterogeneity: single well with +2 SD increased AB metabolism, compared to the other 95 wells, at 3 consecutive time-points.
- Likely due to paracrine signalling



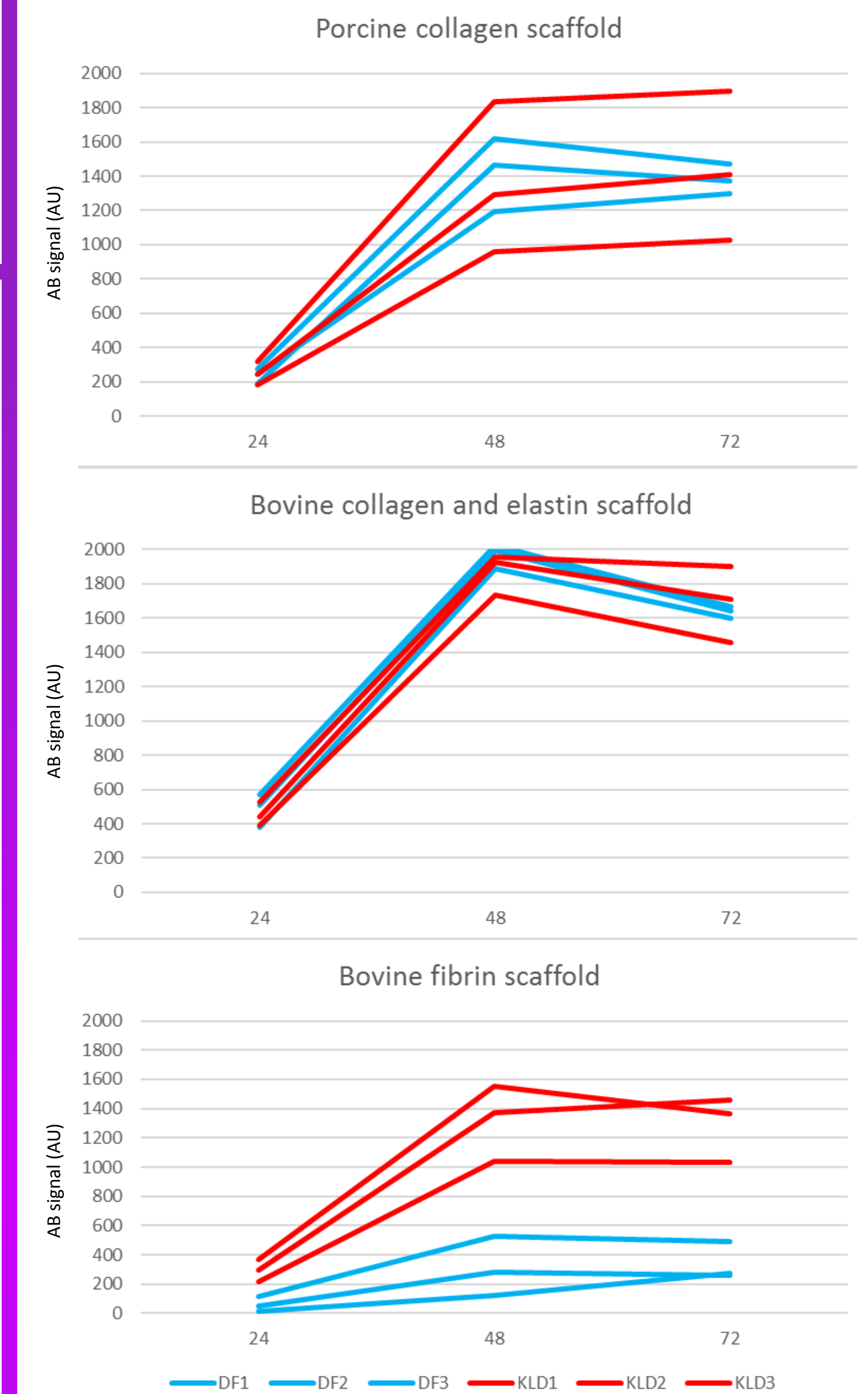
Heterogeneity #2

- Twice as many wells from kFB's are heterogenous compared to NHDFs
- Differences between wells ≠ cell number



Growth in 3D scaffolds

- kFB differential growth reported on chitin derived scaffold⁴
- kFB growth on other natural polymers?
- Differences with NHDF?



→ Marked difference in colonisation on fibrin scaffolds

Conclusion

Keloid fibroblast behaviour is more varied than reported in the literature
Evidence of sub-populations of metabolically distinct cells common to keloid fibroblast isolates: important for scaffold development
kFBs show similar behaviour on natural polymer scaffolds

References

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