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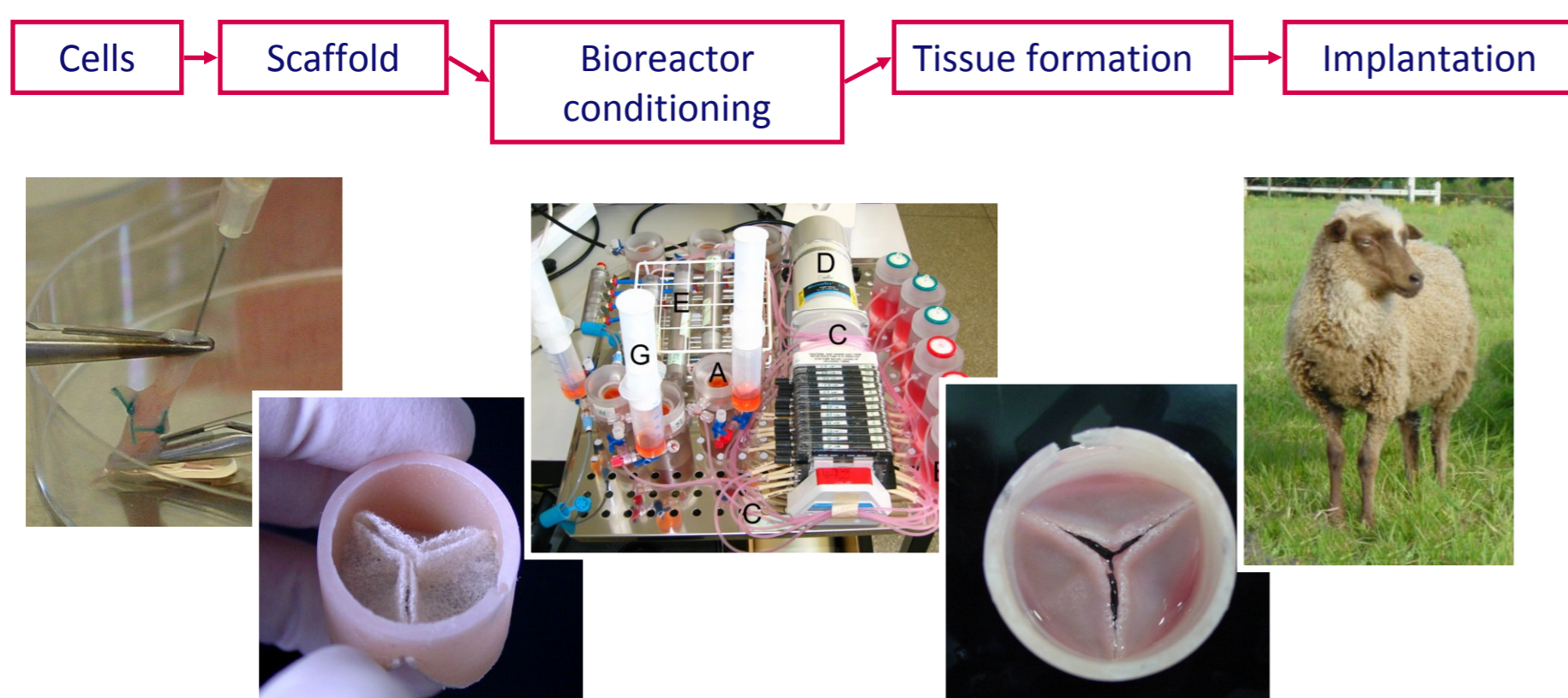
# Variability in ovine tissue engineered heart valves

D. van Geemen, A. Mol, F.P.T. Baaijens, C.V.C. Bouten



## Introduction

Today's heart valve replacements often enhance survival and quality of life, but have several limitations [1]. Most important, these valves do not consist of living tissue and consequently do not grow. Tissue engineering (TE, Fig 1) focuses on developing living autologous heart valve replacements that have the ability to grow, repair and remodel.

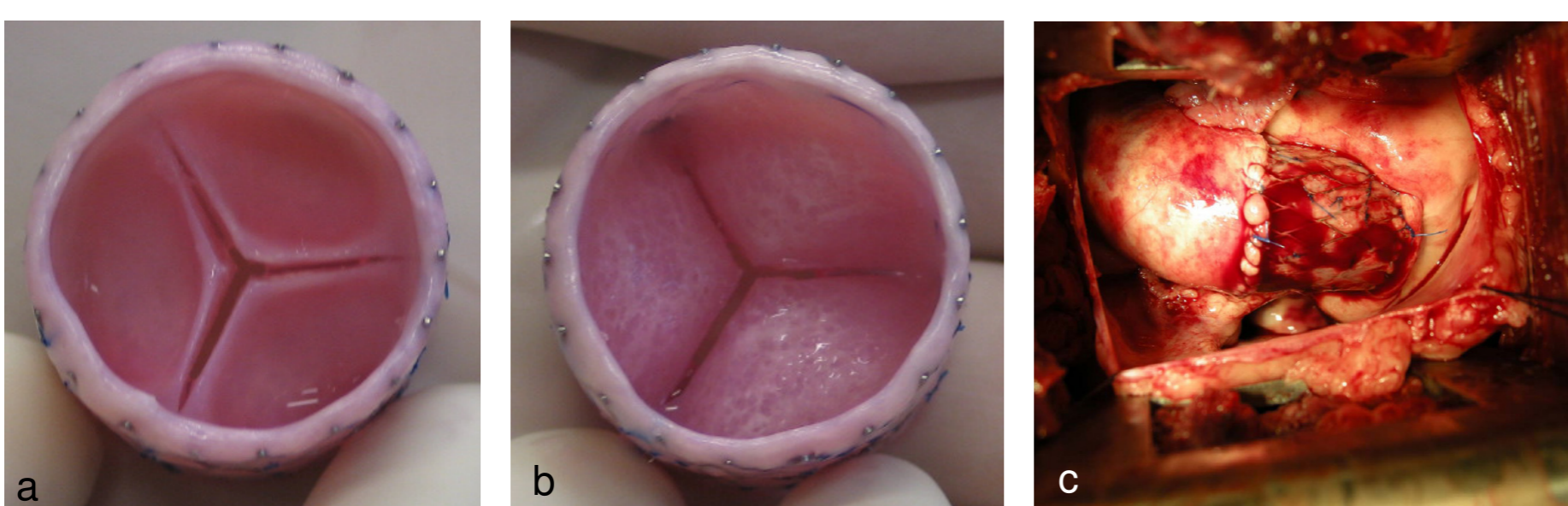


**Figure 1.** The concept of heart valve TE. Venous cells are isolated and expanded in culture prior to seeding them on a biodegradable scaffold. The cell-scaffold construct is then subjected to mechanical triggers in a bioreactor that stimulate extracellular matrix formation until a functional heart valve is grown that can be used for implantation.

To evaluate the in-vivo efficacy of TE heart valves, an ovine model is prescribed. The required cells are isolated from the jugular vein. These cells have shown to produce more extracellular matrix (ECM) and to proliferate faster than other cell sources [2]. However, despite standardized isolation and culture protocols, resulting TE ovine valves show variability in terms of functionality and tissue composition.

## Objective

Investigate the cellular and tissue properties of TE heart valves (Fig 2) using cells from different sheep to unravel the underlying causes of variability in valve outcome.

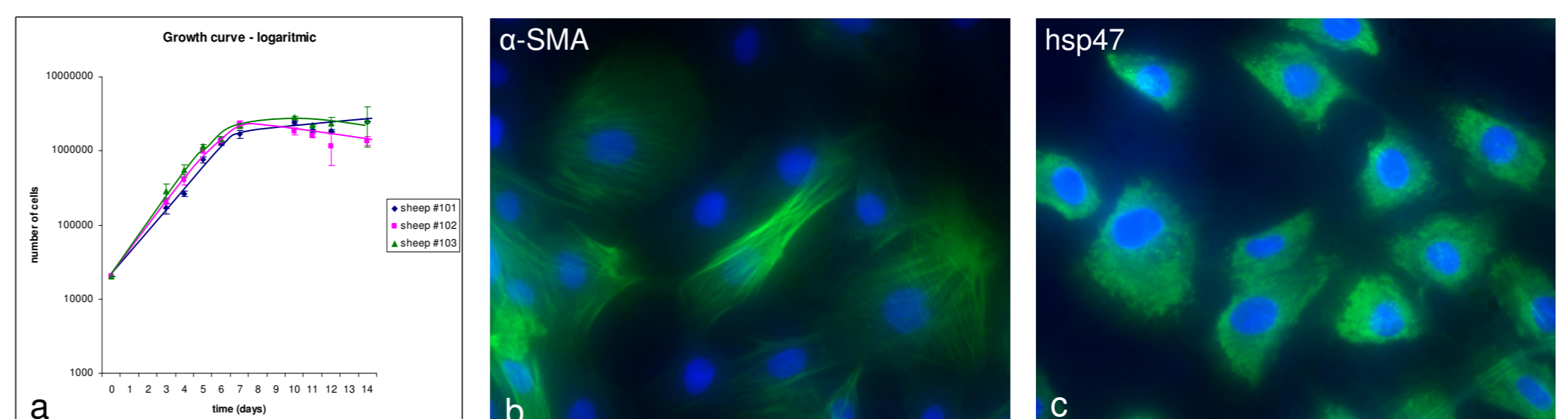


**Figure 2.** Ovine tissue engineered heart valves at top (a), and bottom (b) view, and when implanted at the pulmonary position (c)

## Study approach and first results

**Cellular properties:** Differences in cell proliferation and phenotype will be studied as possible indicators of tissue variability. To study cell proliferation, cell expansion rates will be depicted in a growth curve for each sheep (Fig 3a). Immuno-fluorescence staining will be used for insight into the contractile and matrix forming characteristics of the cells (Fig 3b,c).

**Tissue properties:** ECM composition (collagen, glycosaminoglycans) and cell proliferation (DNA) will be quantified with biochemical assays, whereas tissue morphology will be analyzed by histology. Mechanical properties of the valve tissues will be analyzed by tensile testing. Finally, valve functionality will be studied by interpreting the echocardiogram, which is performed directly after implantation.



**Figure 3.** Studied cell properties: cell proliferation (a), and contractile (b) and matrix forming (c) characteristics

## Discussion

Preliminary results indicate that the cell growth is similar in all sheep (Fig 3a). Therefore, cell growth is probably not the underlying cause in the variability between the ovine tissue engineered heart valves.

The immunofluorescence stainings indicate that a subset of cells is positive for smooth muscle  $\alpha$ -actin (contractile marker, Fig 3b) and all cells are positive for heat shock protein 47 (matrix forming marker, Fig 3c). In future studies, these results will be quantified and correlated to functional performance.

## References

- [1] Mendelson K and Schoen FJ. Annals of Biomedical Engineering 2006;34(12):1799-1819
- [2] Hofmann-Kim et al. Tissue Engineering 2005;11(1-2):288-301

