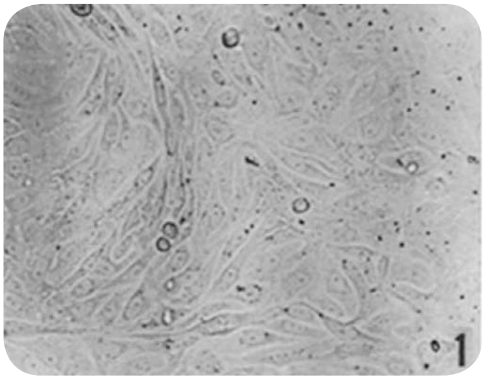
CELLnTEC and a 50 Year Story

The field of epithelial cell culture has been characterised by a series of distinct generations, each with notable advances from those that came before.

Foundation Generation: 1950's and 60's

An era of significant firsts, such as Eagle's Minimum Essential Medium. Although a very simple formulation with only 13 amino acids and 30 ingredients in total, this medium did enable proliferation of certain epithelial cells in vitro, albeit slowly, and without passaging.

In an attempt to speed things up, Dulbecco conducted a basic test in which the concentration of all ingredients were simply multiplied by 4. In this way, Dulbecco's modification of Eagle's Medium (DMEM) was born in 1959.



Kidney epithelial cells, growing in EMEM (Eagle and Freeman, 1958).

1970's. The Co-Culture Generation

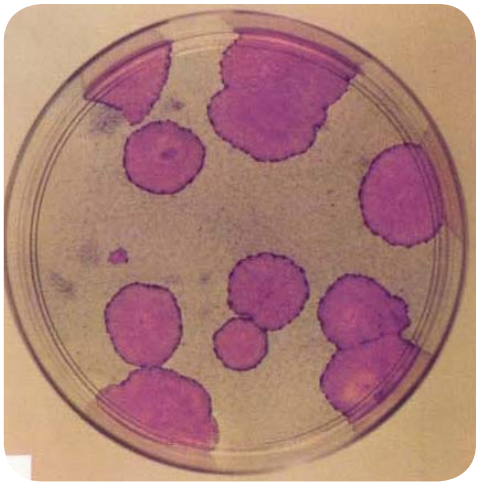
Epithelial cell cultures in the early 70's were slow, with limited longevity, and often contaminated by fibroblasts due to the use of serum.

All three issues were massively improved with one technique: co-culture with irradiated feeder cells.

In the lab of Howard Green, Jim Rheinwald discovered that growing keratinocytes on a layer of irradiated 3T3 mouse fibroblasts in a DMEM-based medium with 20% serum not only improved keratinocyte growth and longevity, but also that the irradiated fibroblasts inhibited fibroblast overgrowth.

Across several publications from 1975 to 1979 the method was improved further to include the use of key growth factors such as EGF, hydrocortisone and choleratoxin.

This method was also combined with the technique of embedding fibroblasts in a collagen matrix (developed by Eugene Bell) to significantly advance the budding field of full-thickness 3D skin cultures.



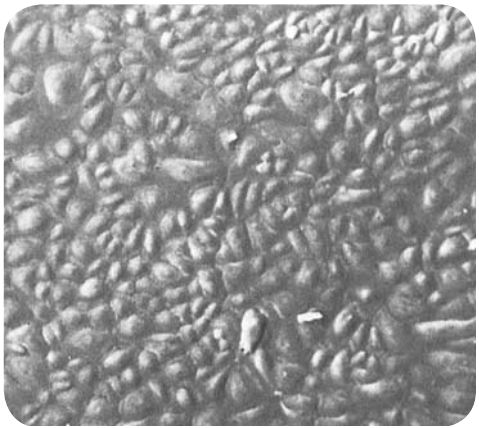
Keratinocytes colonies growing on a bed of 3T3 feeders (Rheinwald and Green, 1975).

1980's: Freedom! (From Serum and Feeders)

Although the co-culture method provided excellent epithelial cell growth, it was complex, time-consuming, and variable due to the serum (in which growth factor combinations often vary by 100-300%!) and fickle feeders.

The 1980's saw serum levels drop down to 10% after improvement of the fundamentally weak DMEM (through combination with F12 medium, thereby increasing the number of components by 60% up to 51), and the addition of factors such as insulin and transferrin.

The long-time work of Dick Ham at the Department of Molecular, Cell and Developmental Biology (MCDB) also lead to the MCDB-153 medium, which with its expanded formulation (55 ingredients) and the use of BPE heralded the end serum dependence in 1982.



Keratinocytes growing in serum free culture using MCDB 153 medium (Boyce and Ham, 1983).

Generation 4: Fully defined media of the 1990's

The early defined media of the 1990's were a key advance on which later generations depended, as all components could be controlled individually.

Culture in a fully defined environment was at last possible with expanded basal media (reaching up to 65 ingredients, including all 20 amino acids, additional vitamins and trace elements), and more comprehensive use of growth factors such as the FGF's.

Although isolation efficiency and longevity in defined conditions did not reach the level of non-defined alternatives, early media (such as Gibco's defined KSFM from the early 1990's) were a significant step forward, as they enabled complete control over every component in the medium – the key for all the more modern media to come.

5th Generation: Stem Cells and Precision Media

Our insight into how different micro environments control specific cell behaviours through a complex network of signalling pathways has advanced considerably since the year 2000.

These insights in combination with fully defined media significantly increase our ability to select specific cell populations, and even to control specific behaviours such as progenitor cell retention, proliferation, differentiation, and aging.

To build a 5th generation family of epithelial cell culture media, CELLnTEC has refined insights from previous generations, and contributed new approaches derived from niche micro-environments, the signalling pathways that control self-renewal, proliferation, and differentiation, and also co-factors to improve growth factor binding.

In this way, the Prime family of media represent the latest chapter in a 50-year story. And the good part? The story isn't finished yet, and the chance to write another chapter still inspires us.

The CnT-Prime media are fully defined, animal component free media that are precisely designed to deliver specific cell behaviours.