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Development of a matrix-based technology platform for the high throughput analysis of 3D cell cultures

Project Number: CTI 18364.2 PFLS-LS
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Main Industrial Partner: FGen GmbH, Dr. Andreas Meyer, René Pellaux, Corinna Hund
Start: 01.01.2017, **Duration:** 24 months

Project goal

The screening of large cell libraries is an important process in pharmaceutical discovery and R&D, e.g. to define drug targets or develop effective medicines. The goal of this project is the implementation of a screening platform based on 3D cultivation of primary human mesothelioma cells encapsulated in alginate hydrogels (Fig. 1) . To this end new hydrogel compositions will be designed, tested and finally utilized in the Nanoliter Reactor (NLR) cultivation system (Fig. 2) that enables high throughput analysis of 3D cell cultures.

Key Findings

- Successful manual cell encapsulation of mesothelioma cell line ZL55SPT into alginate beads (Fig. 1A)
- Life/dead staining of encapsulated ZL55SPT cells (Fig. 1B)

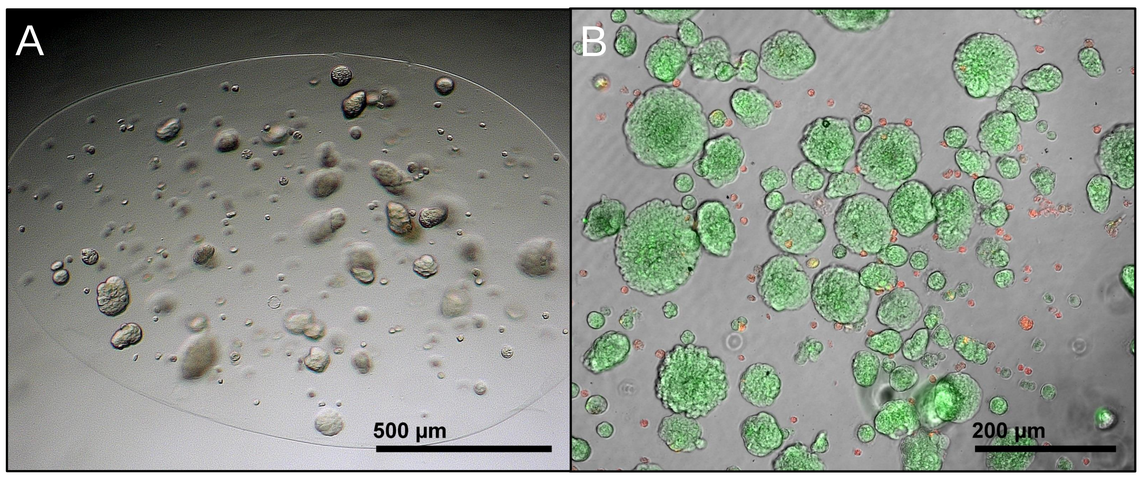

Fig. 1: Mesothelioma cell line ZL55SPT encapsulated in alginate beads. A) Cell growth and spheroid formation after 9 days of incubation. B) Life/Dead staining (green/red) of cells after 21 days of incubation.

Scientific Innovation

- 3D cell culture of mammalian cells in Ca-alginate hydrogels offering different microenvironments:
  - Blending of alginate with natural environment mimicking compounds
  - Modification of the hydrogel stiffness to adapt to native tissue
- Implementation of the modified Ca-alginate hydrogel in the NLR-technology to produce reliable monodisperse capsules at high reproducibility.
- Development of a novel method to generate patient-derived primary mesothelioma cell lines in 3D (e.g. cell subpopulations, like cancer stem cells) from a biopsy in a high throughput manner using the NLR-technology.
- Retain the encapsulated mesothelioma cells in their native state to use them for drug development/treatment to gain predictive drug responses.
- Comparison of *in vitro* to *in vivo* and come up with strategies to develop personalized drug treatment regimes.

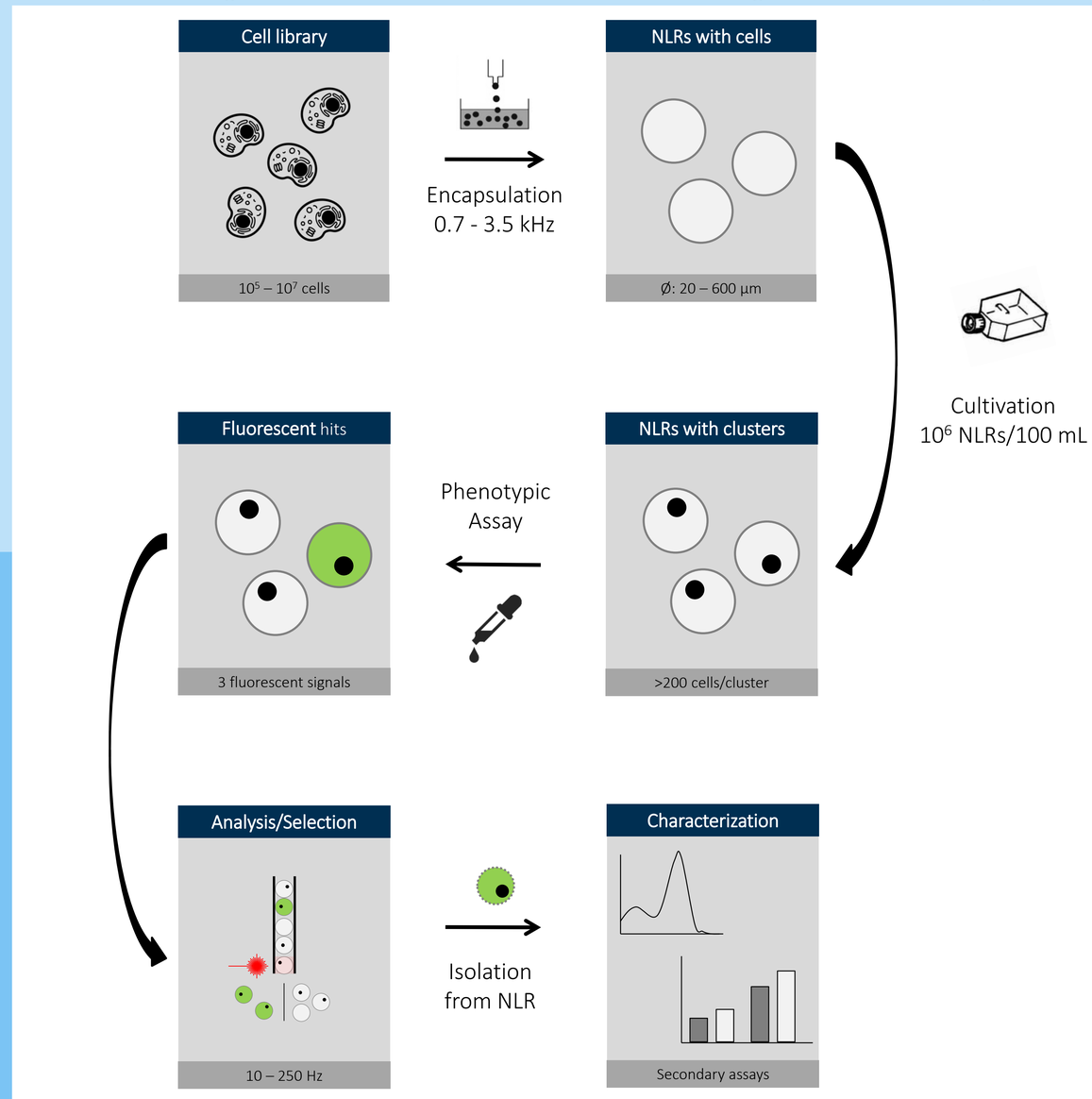

Fig. 2: NLR technology scheme

Business Potential

- New market entry from microbial library screening (industrial biotechnology) to mammalian library screening (pharmaceutical industry)
- High throughput compatible matrix-based 3D cell culture technology
- Primary cell line development
  - Patient-derived cancer (stem) cell lines
- Phenotypic high throughput screening
  - Enrichment of cancer-derived cell subpopulations for targeted therapy
  - Discovery of novel biologics and efficacy and toxicology studies with small molecules

Acknowledgements

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