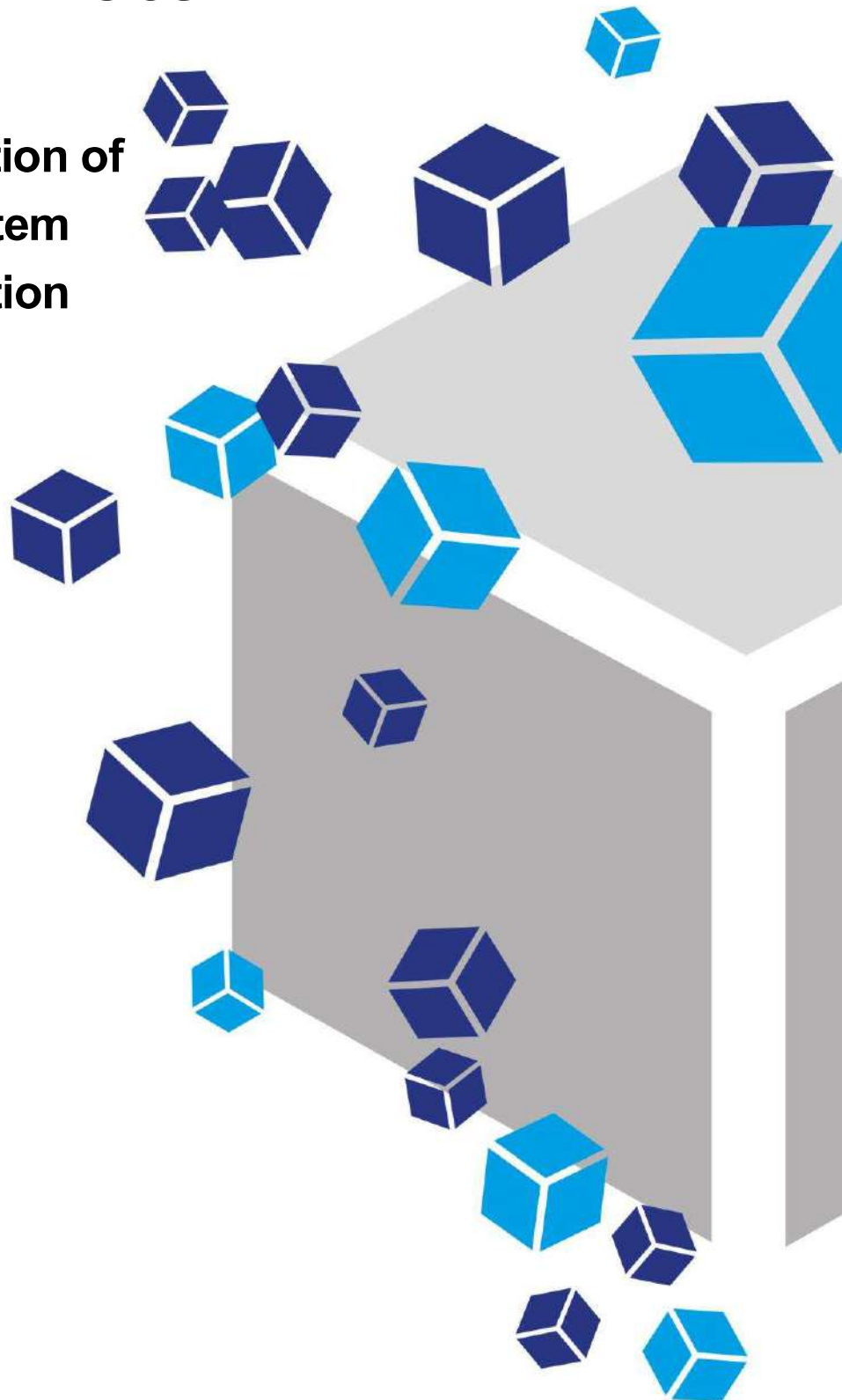


# Application Note

**PODS<sup>®</sup> Activin induction of  
mouse trophoblast stem  
cell aggregate cavitation**



# PODS<sup>®</sup> Activin induction of mouse trophoblast stem cell aggregate cavitation

Data Courtesy of Sarah Harrison and Magdalena Zernicka-Goetz, Cambridge University

## Introduction to PODS<sup>®</sup>

### The challenge for conventional growth factors

Many proteins, especially growth factors and cytokines, when used as a reagent, degrade quickly, rapidly losing their bioactivity. Additionally, they can also suffer from lot-to-lot product variation. This fragility and variability hampers research and significantly limits the therapeutic potential of proteins.

### Protein Micro-depots

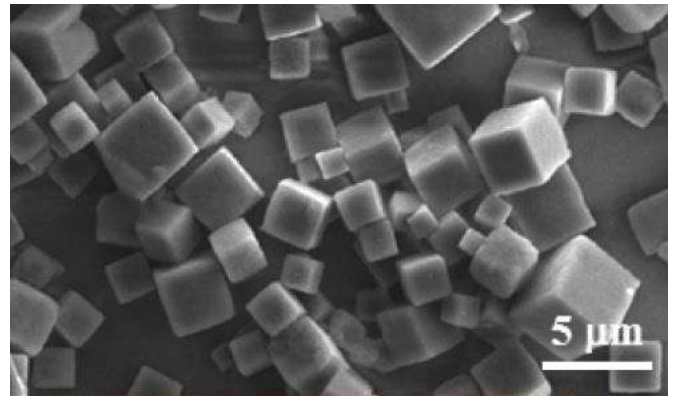
Development of a technology that can continuously replenish active protein from a local, microscopic store, has been a significant challenge, but one that could transform the fields of cell culture and medicine by allowing greater control and reproducibility of cell culture.

### Introducing PODS<sup>®</sup>

PODS<sup>®</sup> is a sustained release system which continuously replenishes proteins from millions of local microscopic stores which can be placed next to (or at a distance from) cells, either randomly or in precise locations. Just like cells, these micro-depots release a steady stream of bioactive protein. This protein can be limited to local surroundings or dispersed more widely, or made to form a gradient.

### How does it work?

At the heart of PODS<sup>®</sup> is an extraordinary polyhedrin protein. This specific polyhedrin protein has the unique ability to encase cargo proteins within perfect, transparent, cubic, micro-sized crystals, much smaller than the cells. These protein crystals form admixtures of the polyhedrin and cargo proteins which slowly degrade, releasing the biologically active cargo protein.



### How can PODS<sup>®</sup> help my research?

PODS<sup>®</sup> are tough and will withstand physical and chemical stress, so you can handle them with ease. PODS<sup>®</sup> typically release intact cargo protein over several weeks and months. Using PODS<sup>®</sup> you can readily create a steady-state protein environment in microscopic detail wherever you want, tailored exactly to your requirements. This is the power of PODS<sup>®</sup>. PODS<sup>®</sup> proteins are now available for many growth factors and cytokines and are already being used in many leading world-class research labs. PODS<sup>®</sup> protein applications include:

- Micropatterning
- Physiological, stable gradient formation
- Bioinks for 3D printing
- Microcarriers
- Functionalizing scaffolds
- Microfluidics (lab on a chip)
- Improved and simplified stem cell culture
- Therapeutic protein delivery

## Overview

Trophoblast stem cell (TSC) aggregates cavitate in the presence of Activin. The data presented here demonstrate the utility of PODS<sup>®</sup> Activin A to induce cavity formation in TSC aggregates.

## Methods

### Aggregate formation

TSC aggregates were generated as described<sup>1</sup> using Matrigel<sup>®</sup>. Single aggregates were transferred into each well in a 96 well plate containing 150  $\mu$ l ETS Embryo media.

### Cavitation

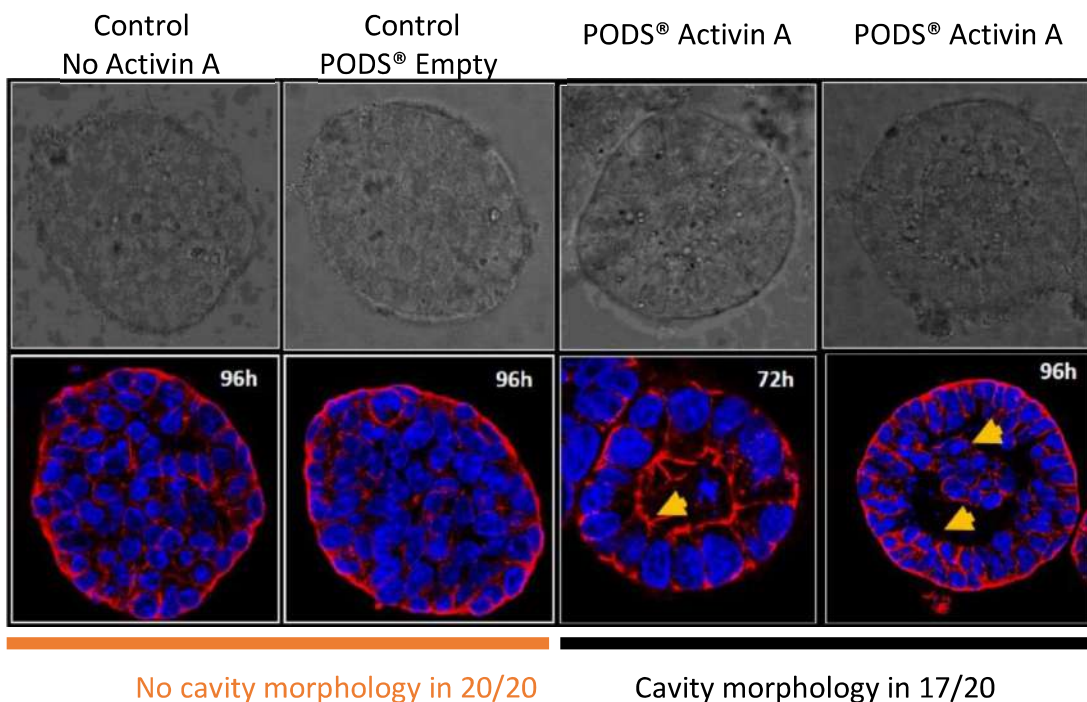
A single dose of  $10^5$  PODS<sup>®</sup> Activin A crystals were added to each well. No further media changes were required. Controls were set up which included no PODS<sup>®</sup> crystals or empty PODS<sup>®</sup> crystals (no cargo protein).

### Immunocytochemistry

Cells were DAPI stained and with an antibody against F-Actin.

## Results

**PODS<sup>®</sup> Activin A treatment supports cavity formation in TSC aggregates.**



**Figure 1. PODS<sup>®</sup> Activin A generates clear cavity formation in a high proportion of TSC aggregates.** Aggregates were examined after 72- and/or 96-hours under fluorescence microscopy for cavity formation. This was observed in 17/20 aggregates treated with PODS<sup>®</sup> Activin A. Cavitation was not detected in any of the aggregates in either of the control groups.

## Conclusions

- PODS<sup>®</sup> Activin A efficiently induces cavitation in mouse TSC aggregates
- Experimental protocols were simplified by the use of PODS<sup>®</sup>

## Reference

Sarah Ellys Harrison, Berna Sozen, Neophytos Christodoulou, Christos Kyprianou and Magdalena Zernicka-Goetz. Assembly of embryonic and extra-embryonic stem cells to mimic embryogenesis in vitro (2017) [Science Vol. 356, Issue 6334](#)

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