



Title	Multi-channel Collagen Gel (MCCG) as a Biomaterial Scaffold for Tissue Engineering [an abstract of dissertation and a summary of dissertation review]
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## Doctoral Dissertation Evaluation Review

Degree requested Doctor of Life Science

Applicant's name KOH Isabel Siew Yin

Examiner :

Chief examiner	Professor Hisashi Haga
Associate examiner	Professor Takayuki Kurokawa
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Title of Doctoral Dissertation

Multi-channel Collagen Gel (MCCG) as a Biomaterial Scaffold for Tissue Engineering  
(組織工学のための生体材料足場としてのマルチチャンネルコラーゲンゲル (MCCG))

Results of Evaluation of the Doctoral Dissertation (Report)

Multi-channel collagen gel (MCCG) is prepared simply by dialyzing a phosphate buffer solution (gelation PBS) against collagen solution, and the phase separation of collagen solution yields a porous anisotropic hydrogel. The anisotropic property of the MCCG is thought to be due to the arrangement of collagen fibres parallel to the circumference of the channel lumen, and perpendicular to the axis of the channel. The aim of this dissertation was to explore the potential of MCCG as a biomaterial for tissue engineering.

The MCCG is a porous hydrogel scaffold onto which cells may be seeded or encapsulated within to achieve a 3D culture system. These seeding methods were tested using single cells and cell spheroids, and it was observed that kidney epithelial cells adhered to the surface of the channels when seeded, but formed cysts with a hollow cavity when encapsulated within the collagen matrix. Furthermore, PC12 cells encapsulated in normal collagen gel (COL) extended more neurites and grew in larger aggregates compared to those in MCCG. These findings suggest that even though various methods have been proposed for 3D culture systems, there still exists differences that affect the way cells behave.

Cell encapsulation techniques typically utilizes the concept of phase separation of a cell-containing polymer solution. The movement of fluorescent particles, used as models of cells, in a phase-separating collagen solution was investigated. The formation of COL proceeds by nucleation and growth (NG) phase separation, while that of MCCG proceeds by spinodal decomposition (SD) phase separation, allowing the study of both types of phase separation simultaneously. The particles were observed to move downwards in COL, and were homogeneously distributed. On the other hand, the particles in MCCG were observed to move mainly sideways and upwards, and were distributed in the collagen matrix region and not in the channels. It was found that the particles do not move in the same way as the phase-separating collagen, but rather is thought to be driven by the movement of water.

The alignment of collagen fibres and the restriction of available collagen-rich regions by the presence of the channels in MCCG make it a prospect for neural tissue engineering, given that the guidance of neurite growth is an important criteria for neural guidance conduits. The alignment of collagen fibres in MCCG was

investigated, and it was shown that the extension of PC12 cell neurites were significantly guided in MCCG compared to COL. It was also suggested that the MCCGs prepared with different ionic concentrations in this study, though having different degrees of collagen fibre alignment, were all within the threshold fibre alignment range required for contact guidance of neurites.

The experiments conducted in this dissertation showed the potential applications of MCCG as a scaffold in 3D culture systems and neural tissue engineering, as well as a tool for studying phase separation processes with relevance to the extracellular matrix (ECM), of which collagen is a major component. Nevertheless, further comprehensive studies are required to fully understand the intricate details about the properties of the MCCG and its formation mechanism.

In conclusion, the author has new findings of the behaviour of cells seeded or encapsulated in collagen hydrogels, as well as the behaviour of particles during the formation of these gels, and these will contribute to the further understanding and development of MCCG as a biomaterial scaffold for tissue engineering.

Therefore, we acknowledge that the author is qualified to be granted a Doctorate of Life Science from Hokkaido University.