14th World Congress on

## TOXICOLOGY AND PHARMACOLOGY March 12-14, 2018 Singapore

## Bridging the MOA and the POC for clinical application: A case study

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Once the manufactured cells were assigned for cell-based medicinal products, non-clinical studies shall be conducted. In the constructed non-clinical study package including *in vitro* and/or *in vivo* studies: (1) the mode of action (MOA) should be shown, (2) the proof of concept (POC) to be acquired and (3) safety of the candidates be examined. In this presentation, we will focus on MOA and POC and bridge these two concepts, in which adipose tissue-derived multi-lineage progenitor cells (ADMPCs) would be developed as cell-based medicinal products for liver fibrosis. To treat the patients with the liver cirrhosis, the pathogenesis and pathophysiology should be concerned to the MOA. Liver fibrosis is characterized by excessive accumulation of extracellular matrix with



inflammatory status *in situ*, therefore, in the developing cell-based medicinal products, anti-inflammatory cytokines and fibrinolytic enzyme secretion is anticipated as MOA. After showing the appropriate MOA, the MOA and the POC should be bridges and the key issues are what kind of animal models should be selected. In the case of the developing cell-based products, MOA is that the cells act as vehicle for the delivery of anti-inflammatory cytokines and MMPs. Tetra carbon chloride ( $CCl_4$ )-chronic induction evolved radicals, followed by inflammation, resulted in fibrosis of the parenchyma. So, the expected mode could be applicable in this animal model. To acquire the POC after bridging to MOA, the appropriate route of administration (ROA) should be concerned. In the case study, the POC of the developing cell-based products by the improvement of liver fibrosis, function by systemic administration of ADMPC. In conclusion it can be said that: (1) MOA should be planned from the pathophysiology of the target diseases, (2) the POC-study should be designed to bridge to the MOA and (3) the applicable limitation should be concerned in clinical use for the patients of the disease.

## **Recent Publications**

- 1. Okura H, Morita M, Fujita M, Naba K, Takada N, Takagaki Y, Suzuki O, Matsuyama A (2017) Therapeutic potential of adipose tissue-derived multi-lineage progenitor cell-sheets on liver fibrosis. *Journal of Translational Science*; 4: 1-6.
- 2. Negoro T, Okura H, Matsuyama A (2017) Induced Pluripotent Stem Cells: Global Research Trends. *Biores Open Access*; 6: 63-73.

## **Biography**

Hanayuki Okura has completed her PhD degree from Osaka University Graduate School of Medicine. She was Research Fellowship for Young Scientists of Japan Society for the Promotion of Science in her graduate school student years. She is currently the Deputy Director of Center for Rare Diseases Research, National Institutes of Biomedical Innovation, Health and Nutrition, Japan.

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