Galunisertib is a promising drug candidate for the treatment of renal fibrosis in ex vivo tissue slice cultures

E. Bigaeva1, E. Gore1, M. Boersema1, H.A.M. Mutsaers1, D. Schuppan2,3, P. Nicklin4 and P. Olinga1

1 Department of Pharmaceutical Technology and Biopharmacy, University of Groningen, Groningen, The Netherlands.
2 Institute of Translational Immunology and Research Center for Immunotherapy, University Medical Center, Mainz, Germany
3 Division of Gastroenterology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA
4 Boehringer Ingelheim, Biberach, Germany

**Background**

- Precision-cut kidney slices (PCKS) culture is an ex vivo model that replicates most of the multicellular characteristics of a whole organ in vivo. Moreover, PCKS can be prepared from murine and human, healthy and diseased tissues, while the cells are retained in their original environment.
- Galunisertib (Galu; LY2157299) is an inhibitor of TGFβR1 kinase that is currently being investigated in clinical trials as an anticancer drug. Therefore, Galu is a potential candidate for fibrosis treatment.
- This study aims to elucidate the effects of Galu on the early and end stages of fibrosis using PCKS from murine and human tissue.

**Materials and Methods**

- **Viability of PCKS:**
  - ATP content

- **Gene expression of fibrosis markers:**
  - Collagen 1α1 (Col1α1)
  - Heat Shock Protein 47 (HSP47)
  - α-Smooth Muscle Actin (αSMA)
  - Fibronectin

- **Results**

  **Mouse PCKS**

  - **Healthy (n=3)**
  - **Fibrotic (UUO 7 days) (n=4)**

  **Human PCKS**

  - **Healthy (n=5)**
  - **Fibrotic (n=3)**

  **Conclusions**

  - Galunisertib exhibits strong antifibrotic activity in the early and end stage of fibrosis in mouse and human PCKS.
  - The PCTS technique is a promising model to test antifibrotic agents both in rodent and human tissues, considering the latter as a bridge to clinical studies.

To read more about precision-cut tissue slices, scan this QR code with your smartphone.