KIDNEY FAILURE and EDEMA

Background

Edema forms in patients with kidney disease for two reasons:

1. A heavy loss of protein in the urine
2. Impaired kidney (renal) function

In this situation, the patients have normal or fairly normal kidney function. The heavy loss of protein in the urine with its accompanying edema is termed the nephrotic syndrome. Nephrotic syndrome results in a reduction in the concentration of albumin in the blood (hypoalbuminemia). Since albumin helps to maintain blood volume in the blood vessels, a reduction of fluid in the blood vessels occurs. The kidneys then register that there is depletion of blood volume and, therefore, attempt to retain salt. Consequently, fluid moves into the interstitial spaces, thereby causing pitting edema.

Podocytes are essential for normal functioning of the glomerular filtration barrier (GFB) of the kidney. Damage or loss of podocytes causes glomerulosclerosis nephrotic syndrome in humans. In fact, disruption of the GFB is characterized by proteinuria, hypoalbuminemia, edema, and hyperlipidemia.

Pathology Model

In order to evaluate the anti-inflammatory activity of CLIENT's compounds, human podocytes will be challenged with selective in vitro noxious stimuli mimicking renal failure and quantitative evaluation of podocyte viability will be monitored.

In particular, a conditionally immortalized human podocyte cell line will be cultured at 33°C in their undifferentiated status, then differentiated at 37°C. Cells will be challenged with either H2O2 (in order to mimic oxidative stress) or endothelin (in order to mimic endothelial conditioned podocyte damage).

Readouts

The following parameters will be taken into consideration:

- Viability of podocytes
- Quantitative evaluation of metabolic activity
- Evaluation of oxidative stress (i.e. ROS production)
- Quantitative evaluation of mitochondrial damage