【Symposium 6-1】

Drug delivery by nanoparticle in kidney disease

Hui-Teng Cheng

鄭暉騰

Department of Internal Medicine, National Taiwan University Hospital Hsin-Chu Branch

新竹台大醫院 腎臟科

Kidney-specific delivery of therapeutic agent by nanocarrier is a promising strategy to potentiate the treatment effect and minimize the off-target toxicity. This review aims to identify the nanocarriers that may preferentially accumulate in the kidney, and compare the efficacies among various cargo-carrier combinations. Particle size plays a decisive role in determining its intrarenal location. Nanoparticles smaller than 2 nm tend to be entrapped within the glomerular filtration barrier, while those with sizes 5 nm to 130 nm are ready to pass through the barrier. For those smaller than 100 nm, smaller ones are more likely to enter the urinary space and get caught by the tubular epithelial cells, but the larger one tends to retain within the glomeruli or the mesangium. For those larger than 100 nm, the glomerular deposition is diminishing. Those with size ranging from 130 nm to 300 nm do not stay in the kidney, and those smaller than 250 nm tend to retain in the liver. Those with size approximately 350 nm to 400 nm can go across the peritubular capillary endothelial cells and reach the tubular epithelial cells. Certain nanocarrier platforms including nanocarbon, DNA origami nanoraft, and meso-scale nanoparticle display high kidney specificity. Nanocarriers that utilizes receptor-ligand interaction to facilitate kidney specific delivery include those conjugated with kidney-specific peptides (KKEEE)3K and CLPVASC, lysozyme, the elastin-like polypeptide, dendrimer conjugated with L-serine that interacts with Kidney Injury Molecule-1 on injured tubular epithelial cells, and chitosan-coated nanoparticles to bind megalin on the proximal tubular epithelial cells. Maximal efficacy in treatment of experimental acute kidney injury may be achieve by anti-oxidants conjugated with dendrimer or sialic acid-dextran, or by black phosphorus nanosheet as an anti-oxidant itself. Podocyte- and myofibroblast-targeting nanocarriers need to be developed. This review aims to identify the nanocarriers that may preferentially accumulate in the kidney, and quantitatively compare the efficacies among various cargo-carrier combinations.