Washington University in St. Louis
Office of Technology Management

MRI AND PET NANOPARTICLE IMAGING AGENTS FOR KIDNEY DISEASE DIAGNOSTICS AND TRANSPLANT EVALUATION

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Technology Description:

Researchers at Washington University in St. Louis have developed targeted, natural nanoparticle imaging agents that may be used to quantify kidney nephron endowment and diagnose renal disease with MRI or PET imaging.

Nephrons are the functional units of the kidney responsible for removing waste from blood. Nephron number decreases with age and loss of nephrons is associated with development of kidney disease. Current techniques to monitor nephron number are inaccurate or require an invasive biopsy. To overcome these drawbacks, the inventors developed a human recombinant form of cationic ferritin (HrCF). Cationic ferritin (CF) is a natural iron-oxide nanoparticle MRI contrast agent that binds to microstructures in the kidney and enables measurements of nephron endowment. Because HrCF is based on an endogenous human protein, it is more likely to be compatible with use in humans than previous CF agents from horse spleen. Furthermore, HrCF can be easily produced in *E. coli* with controlled iron loading, allowing for rapid synthesis of a functional agent. HrCF can also be adapted as a PET tracer (RadioCF) by labeling with CU-64. This technology could provide a tool for non-invasive quantification of nephrons in living patients to potentially enable evaluation of human kidney allografts or early diagnosis of renal disease.

Stage of Research:

- **Proof-of-concept** – The inventors synthesized human recombinant cationic ferritin nanoparticles in *E. coli* and demonstrated its use as a targeted renal imaging agent in MRI studies to calculate nephron endowment in mice.

Applications:

- **Imaging agents for PET or MRI** to diagnose and monitor kidney disease by assessing nephron endowment in:
  - patients at risk for kidney disease
  - transplant donors

Key Advantages:

- **Targeted, natural, nanoparticle agent**
  - recombinant endogenous/human-based ferritin protein has higher likelihood of biocompatibility (compared to previous horse spleen ferritin)
  - readily functionalized with modifiable core
  - regulated iron loading could result in better in vivo performance
  - for PET tracer – micro-dose detection to reduce potential toxicity and rapid radiolabeling to minimize radioactive decay before imaging
- **Non-invasive imaging** to quantify glomerular number, with potential to replace traditional biopsy

- **Rapid, low-cost production in bacteria**

Patents: Compositions of and methods of making ferritin-based imaging agents (PCT Publication No. WO202018105)

Publications:

- Imaging agent may help gauge kidney health. *The Source,* (2021) Washington University in St. Louis.
- Charlton JR, Baldelomar EJ, Hyatt DM, Bennett KM. Nephron number and its determinants: a 2020 update. *Pediatr Nephrol.* 2020 Apr 29. Online ahead of print.
- Bennett KM, Baldelomar EJ, Morozov D, Chevalier R, Charlton JR. New imaging tools to measure nephron number in vivo: Opportunities for developmental nephrology. (Invited Review). *J Dev Orig Health Dis.* 2020 Jan 27:1-5. Online ahead of print.
- Baldelomar EJ, Reichert D, Shoghi KI, Beeman SC, Charlton JR, Strong L, Fettig N, Klaas A, Bennett KM. Mapping nephron mass in vivo using positron emission tomography. *Am J Physiol Renal Physiol.* 2020 Dec 7. Online ahead of print.

Related Web Links: Dr. Kevin Bennett profile