

# **Nanoprobes for *in vivo* drug toxicity imaging**

Researchers in Dr. Jianghong Rao's lab have developed nanoprobes for monitoring drug-induced hepatotoxicity *in vivo* in real time. Drug toxicity is a long-standing concern of modern medicine. Oxidative and nitrosative stress underlie drug toxicity due to the metabolic bioactivation of drugs to reactive metabolites. The liver is the organ most frequently affected. In addition to effects on the end-user, drug-induced hepatotoxicity is the single most important cause of both FDA non-approval and drug withdrawal from the market. Current preclinical methods to predict drug toxicity are limited as they cannot be used in live animals and do not analyze biomarkers that are mechanistically linked to the toxicity of the parent drug compound. To overcome this limitation, the inventors designed this nanoprobe which measures oxidative and nitrosative stress and thus can uniquely image drug toxicity in real time in live animals.

## **Stage of research**

The nanoprobe was used in mice for real-time *in vivo* monitoring of hepatotoxicity following challenge with two known hepatotoxic drugs. The imaging results were validated with histological analysis.

## **Applications**

- Drug development
  - Drug safety screening
    - Screen new drugs or chemical entities for their propensity to produce hepatic oxidative or nitrosative stress
  - Drug toxicity studies
    - Obtain mechanistic information about drug toxicity
    - Selection of remediation strategies
    - Aid in redesign of drug candidates

- Basic research

## Advantages

- Superior optical reporter
  - Resistant to oxidative chemical bleaching effects (unlike quantum dots or small molecule fluorophores)
  - Stable
  - Biocompatible
  - Permits longitudinal studies *in vivo*
- Simultaneously and differentially detect two sources of toxicity to permit
  - More comprehensive toxicity screens
  - More robust assessment of mechanism of toxicity
- Can be tailored for specific analyte detection and for targeting to specific organ of interest
- Reduce risk in drug development
- Improve therapeutic outcomes and patient safety

## Publications

- U.S. Patent No . [9,849,198](#).
- Shuhendler et al. [Real-time imaging of oxidative and nitrosative stress in the liver of live animals for drug-toxicity testing](#). Nat Biotech published March 23, 2014 on-line.
- Moskvitch, K. [Nanoparticle sensors detect drug damage in the liver](#). Chemistry World. March 26, 2014.
- Pu, K., Shuhendler, A. J. and Rao, J. (2013), [Semiconducting Polymer Nanoprobe for In Vivo Imaging of Reactive Oxygen and Nitrogen Species](#). Angew. Chem. Int. Ed., 52: 10325–10329. doi: 10.1002/anie.201303420

## Patents

- Published Application: [20150011878](#)

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