## Metal Oxide Nanoparticles Encapsulated in Porous Polymer Microparticles for Modulating Hydrogen Sulfide Concentrations Towards Colorectal Cancer Treatment

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*Fusobacterium nucleatum* is a key exogenous hydrogen sulfide (H<sub>2</sub>S) producer in the bowel. The concentration of H<sub>2</sub>S in healthy people ranges from 250  $\mu$ m – 3.4 mM<sup>1</sup> and is significantly higher in people with bowel conditions such as inflammatory bowel disease (IBD) and colorectal cancer (CRC).<sup>2,3</sup> People with CRC are unable to effectively detoxify H<sub>2</sub>S.<sup>4</sup> Bismuth subsalicylate, a current treatment for reducing H<sub>2</sub>S in the colon, is not recommended for long-term use due to risk of severe neurological side effects.<sup>5</sup> We present metal oxide nanoparticles encapsulated in porous polymer microparticles that are capable of adsorbing H<sub>2</sub>S via a simple reaction where water is the sole by-product (Eq. 1). CuO nanoparticles (50 nm) were encapsulated within porous poly(methyl methacrylate) (PMMA) microparticles (PMMA/CuO particles) via a water-in-oil-in-water double emulsion. The PMMA/CuO particles have an average diameter of 465 ± 25  $\mu$ m and ~2-10  $\mu$ m pore size (Fig.1A). Methylene blue assay confirmed that clinically relevant amounts of PMMA/CuO particles (2 mg with 5 wt.% CuO) can adsorb 98% of H<sub>2</sub>S produced by *Fusobacterium nucleatum* within 60 min (Fig.1B). These particles may prove useful in the prevention and treatment of exogenously elevated H<sub>2</sub>S levels in bowel conditions and CRC.

$$H_2S + CuO \rightarrow CuS + H_2O \tag{1}$$



**Figure 1: (A)** Scanning electron microscopy micrographs of PMMA/CuO particles; Scale bar: 1 mm (top) and 10  $\mu$ m (bottom). **(B)** Percentage of H<sub>2</sub>S adsorbed by 2 mg/mL PMMA/CuO particles over time (15, 30, and 60 min). H<sub>2</sub>S was produced by incubating ~1.4 x 10<sup>8</sup> *Fusobacterium nucleatum* with 20 mM L-cysteine for 30 min.

## **References:**

<sup>1</sup> Attene-Ramos, M. S.; et al. Environ Mol Mutagen 2010, 51, 304-314

- <sup>2</sup> Blachier, F.; et al. Am J Physiol-Gastrointest Liver Physiol 2021, 320, G125-G135
- <sup>3</sup> Kanazawa, K.; et al. Cancer 1996, 77(8 Suppl), 1701–1706.
- <sup>4</sup> Ramasamy, S.; Am J Physiol-Gastrointest Liver Physiol 2006 291(2), G288–G296.
- <sup>5</sup> Gordon, M. F.; *Mov Disord* **1995**, *10*(2), 220–222.