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Entrapping digestive enzymes with engineered silica particles reduces metabolic risk factors – evidence from preclinical and clinical investigations

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Mesoporous silica particles (MSPs) are thermally and chemically stable porous materials composed of pure silica and have attracted substantial attention for their potential uses in biomedical applications1,2. By carefully tailoring the MSP characteristics (controlled surface area, pore volume, pore size, particle size and morphology), we have engineered a silica particle (SiPore15™) that efficiently entraps key gastrointestinal digestive enzymes. Preclinical investigations illustrate how pancreatic lipase and α-amylase are sequestered by SiPore15™ *in vitro*. This phenomenon is also demonstrated in a mouse intestine model *ex vivo*, where the enzyme activity in the SiPore15™ exposed murine duodenal fluid is substantially decreased[3]. We hypothesize that SiPore15™ acts by lowering the enzyme activity in the small intestine, subsequently resulting in decreased digestion of macronutrients, leading to reduced calorific uptake at the organism level 4. To date, 60 human subjects have been orally treated with 9 g/day of SiPore15™. A First-in-Man (FiM) trial has been completed with healthy volunteers (n=10) and obese participants (n=10). The clinical effects observed in the obese participants were significant reduction in metabolic and cardiovascular risk factors such as HbA1c (net reduction of 1.7 mmol/ml, - 5%) and LDL-cholesterol (net reduction of 0.4 mmol/L, - 15%). The observed adverse events were mild and transient 5. SiPore15™'s innovative mode of action, combined with the effects observed in obese subjects and the promising safety profile, makes SiPore15™ an exciting candidate for treatment/prevention of metabolic diseases. A second trial with prediabetic/type 2 diabetes patients (n=40) is ongoing and the results will be reported in the second half of 2019 (clinicaltrials.org ID no. NCT03823027).

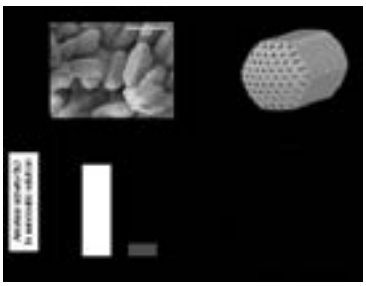

Figure legend: A closer look at SiPore15™

References:

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2. McCarthy (2015), Mesoporous silica formulation strategies for drug dissolution enhancement: a review. Expert Opin Drug Delivery 13(1):93-108.

3. Rollman-Waara, Engineered silica particles reduce metabolic risk factors in humans by entrapping digestive enzymes. In manuscript.
4. Kupferschmidt N (2014), Large pore mesoporous silica induced weight loss in obese mice. Nanomedicine 9(9):1353-62.
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Biography

Erik Waara received his PhD. from Karolinska Institutet, Stockholm, Sweden in 2004 after performing preclinical HIV vaccine research, under the supervision of Prof. Britta Wahren. In 2005, he joined Prof. Stephen J Kent's laboratory at the University of Melbourne, Australia, where he worked on virus induced cellular immunity, studies supported by the Swedish Research Council. Upon returning to Sweden in 2008, he joined BioArctic AB as a senior researcher where he spent almost 10 years conducting hands-on pre-clinical research and development, generating antibody-based biotherapeutics in the fields of Alzheimer's and Parkinson's diseases. In September 2017, he joined Sigrid Therapeutics AB as Head of Pre-Clinical Development.

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