Fraunhofer IZI

Fraunhofer Institute for Cell Therapy and Immunology IZI

Detoxification agents

Department of Extracorporeal Therapy Systems

The removal of toxic substances from organisms becomes essential when organs inadequately detoxify or excrete harmful substances. Dysfunction of organs such as liver and kidneys, as well as a disrupted intestinal barrier, is accompanied by the accumulation of substances like uremic and endogenous toxins or enterotoxins in the blood and tissue. This in turn triggers pathological processes that lead to e.g. chronic renal failure or gastrointestinal diseases. These common diseases are associated with an increased morbidity and overall mortality.

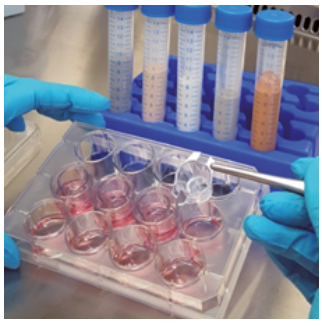
Removal of toxic substances is an important issue for numerous clinical indications. Therefore, the development of effective and biocompatible sorbents to compensate organ dysfunction is a promising approach for the above mentioned indications.

Research into novel detoxification agents will help to expand the spectrum of therapeutic options and improve existing concepts.

The Department of Extracorporeal Therapy Systems develops in vitro screening models and test systems for the evaluation of innovative sorbents and detoxifying agents.

Focus

Our current research activities focus on members of the silicate and smectite group of clay minerals. These substances display unique adsorption characteristics, which make them very promising candidates for various detoxification challenges.



Specific in vitro tests revealed the potential of Montmorillonite illite clay minerals and other sorbents for the binding of relevant harmful substances like uremic toxins, as well as entero- and bacterial endotoxins. This potential could also be verified in subsequent in vivo screenings.

Inflammatory bowel disease

Inflammatory bowel disease (IBD) is a chronic relapsing inflammatory condition of the gastro-intestinal tract. IBD patients need lifelong medication which often leads to serious side effects. Therefore, treatment of IBD and the exploration of novel therapies represent an important research field.

We established a short-term-intestinal-bowel model that could serve as an experimental test system, which enables the investigation of early mucosal inflammation of IBD pathogenesis and the rapid screening of novel therapeutic options.

We proved the beneficial effects of smectite clay minerals on inflammatory processes in a short-term model as well as in an acute dextran sodium sulfate (DSS)-induced model. Furthermore, prophylactic smectite application alleviated the clinical signs of DSS-induced colitis, possibly mediated by barrier strengthening processes and intestinal microbiome modification.

These studies indicated that smectites are a novel therapeutic and prophylactic option for IBD-treatment.

Chronic renal failure

Chronic kidney disease (CKD) is highly associated with elevated serum phosphate levels contributing to vascular calcification and an increased cardiovascular risk in dialysis patients. Reduction of hyperphosphatemia is the main therapeutic target, and the finding of novel phosphate binding agents is an essential research area.

We investigated the phosphate binding capacity of modified, highly phosphate affine smectites and their impact on phosphate induced cellular calcification processes in an in vitro cell culture model of human coronary artery smooth muscle cells. Furthermore, application of phosphate adsorbing smectites in a rat model of CKD resulted in (i) significantly reduced pathology in their vasculature, (ii) lowered microalbuminuria, which is a prognostic marker for cardiovascular events, and (iii) finally increased the survival of renal insufficient rats.

Due to the high phosphate affinity of smectites and the resulting lowered vascular pathology in CKD rats, this study indicates that smectite is a potent phosphate absorber, comparable to established clinical therapeutics.

Equipment

The Department of Extracorporeal Therapy Systems is well equipped for the characterization of detoxifying agents:

- Cell culture facilities
- Animal models
- Histology equipment
- Fluorescence microscopy

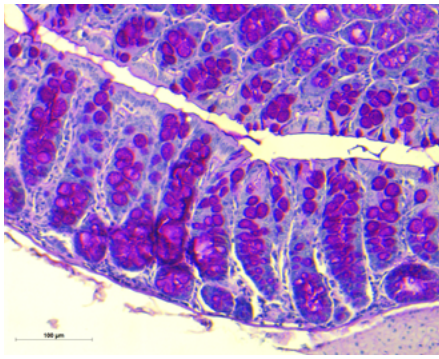
Due to a broad network of cooperation partners, the group also has access to additional state-of-the-art technologies. In addition, the cooperation with various clinical departments (such as gastroenterology, nephrology, microbiology) of the University Medicine Rostock enables clinically oriented research of new therapeutic strategies.

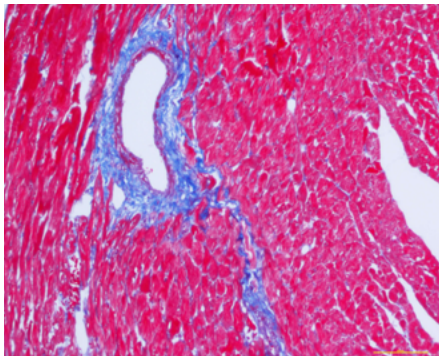
IP situation

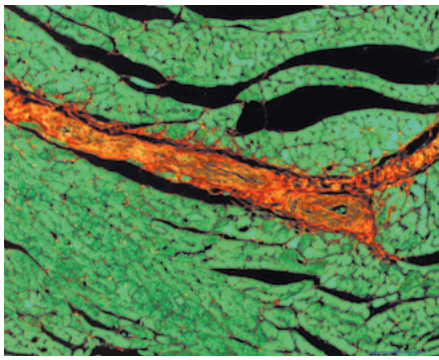
We patented the use of mineral compounds for the application in inflammatory bowel disease and for the reduction of serum phosphate caused by chronic renal failure.

Selected references

Breitrück et al., 2013. **Establishment of a novel extracorporeal bowel model to study luminal approaches to treat inflammatory bowel disease.** Disease Models and Mechanism : 1487-1493.







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