Given the rising cost of providing healthcare services coupled with the increasing average age of the population, modern medical practice needs to focus its attention on preventive diagnostics, reliable techniques for the monitoring of disease progression and responses to treatment, and efficient therapies. In order to develop solutions to these requirements, there is an imperative need for intelligent low-cost material alternatives. For high-sensitivity in-vivo and in-vitro diagnostic and therapeutic applications, the business unit Health of Fraunhofer ISC has come up with a novel concept for the design of customized particle systems, which bears the name ORMOBEAD®¹.

ORMOBEAD® stands for a new generation of multifunctional particle systems and for an all-round concept that is based on variable structural units and therefore able to provide solutions for even the most complex requirement profiles. The modular structure of the core/shell-type ORMOBEAD® particle systems offers a maximum of flexibility with regard to size, materials, effective targeting, and type of medical imaging technique. The resulting ORMOBEAD®s can bind to biomarkers or deliver drugs and are visible to different types of imaging systems. There are variations for in-vivo and in-vitro use.

¹ ORMOLX®: Registered trademark of the Fraunhofer-Gesellschaft für Angewandte Forschung e. V.
Synthesis

- conducted by wet-chemical methods using sol-gel technology
- elegant design strategy: »building block« principle
- doping of particle matrix possible with various organic dyes or rare-earth ions to adjust luminescence properties

Particle properties

- Narrow particle size distribution
- High particle stability in various environments

Adjustable properties:
- composition
- size
- crystal structure
- optical properties
- refraction index

Surface modification

Subsequent to the particle fabrication reactive functionalities are introduced to the surface by conventional functionalization methods.

Available surface modifications:
- carboxyl
- amine
- mercapto
- isocyanate

The spacer length and type of chemical functionality are systematically adapted to the intended application and allow adaptation into different environments or matrix materials.

The particle surface coverage with chemical functionalities is analyzed qualitatively and quantitatively.

Biofunctionalization

Covalent and non-covalent attachments of biological moieties take place by standard bioconjugation methods.

The oriented conjugation of biomolecules included:
- antibodies
- nucleobases
- selected proteins

The functionality of the bound biomolecules is verified by subsequent biological tests.

ORMOBEAD® concept for the fabrication of customized multifunctional particles

Core/shell-structured particles on the basis of silicates and calcium phosphates under excitation with UV-lamp ($\lambda_{\text{exc}} = 254 \text{ nm}$)