

FRAUNHOFER ATTRACT 3DNANOCELL



 Analysis of protein activity in Arp2/3 labelled cell, wrapping around a 3D post structure
Graphic visualization of analysis approach: Living cell migrating into force sensor nanopost field
SEM micrograph of fixed cell flexing a force sensor nanopost
Extraction of the temporal evolution of nanopost deflection for cell force calculation

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CUSTOMIZED 3D CELL ASSAYS FOR DRUG SCREENING

A rapidly progressing demographic change and the need for better treatments call for faster and more efficient ways of drug development – to increase profitability and shorten time-to-market. Animal testing is ethically critical and economically arguable: ~ 80 % of the substances tested as effective on mice turn out to be ineffective in humans. Novel approaches for reliable and safe high-throughput preclinical tests are key issues to speed up drug development.

All-in-one 3D-Assay and Analysis Development

Fraunhofer Attract 3DNanoCell develops cell-based 3D assays in cell-type specific environments mimicking physiological conditions. This enables the precise study and analysis of interactions between biological systems and active substances or substrates required for drug screening and other pharmaceutical applications. To this effect, we synthesize, structure and functionalize materials, customize reliable and efficient analysis methods and design in-vitro studies tailor-made for human cell types.

We provide solutions for every aspect during the development of drug screening assays:

- 3D structured environments and patterned surfaces – tunable at the micron- and nanoscale
- Dynamic cell culture-assays with spatiotemporally controlled stimuli
- Live cell imaging and biochemical readout
- Application-specific data analysis

Located at the very center of the unique scientific infrastructure at Fraunhofer ISC, 3DNanoCell offers various advantages as your partner for pharmaceutic research: Cooperation of scientists from diverse disciplines – including physics, chemistry, biology, materials science and nanotechnology – is combined with easy access to sophisticated



technologies for the effective realization of biological and medical R&D projects.

We are **your partner for all-in-one process development** covering consulting, material design, cell culture, cell stimulation, advanced data analysis – all services GMP/GLP compliant.

We develop 3D assays for pharmaceutic objectives including:

- Drug efficiency tests
- Development and analysis of drug delivery systems
- Endocytosis and intracellular transport
- Cell adhesion and proliferation on drug-loaded scaffolds
- ... or your specific application.

3D Structured Environments

To mimic physiological surroundings of specific cell types, we realize complex 3D environments comprising features at the micron- and nanoscale by employing various bottom-up and direct structuring methods – including two-photon polymerization (TPP), nano imprint, 3D printing and printed electronics. By chemical functionalization, we tune structured surfaces to match the targeted application and our design processes are supported by finite element simulations.

These techniques allow for the generation of assays mimicking the long-range threedimensional patterns of human tissue ¹ and the short-range surface interactions by nanotopographies or protein-coating ². A relevant example is the migration of tumor cells in a complex 3D environment to evaluate the metastatic potential and to test the inhibi-tion of metastasis under the influence of different drug candidates.

Dynamic Cell Culture – Assays with Variable Stimuli

In tailored cell-type specific assays spatiotemporally variable stimuli are applied to influence cell behavior:

- Cell force sensors Measurement of exerted cell forces (e.g. matrix deformation by metastatic cells) (see figures 1- 4)
- Advanced microfluidic setups ³ Drug administration and chemotaxis assays at the micron scale, mimicking of fluid flows in the human body
- Micro-actuators Mechanical cell stimulation (e.g. imitation of heartbeat or breathing)
- Tweezer technology Controlled positioning of nanoparticles or -carriers

Live Cell Imaging and Biochemical Readout

In our Imaging Center, cell behavior in 3D assays ⁴ is assessed by live cell microscopy techniques, which include spinning disk confocal microscopy (SDCM) and confocal laser scanning microscopy (CLSM) as well as super-resolution techniques like STED, STORM and Palm. Additionally, we perform biochemical investigations, e.g. for cytokine expression in immune response assays.

Application-specific Data Analysis

Application-specific analysis algorithms are one of our key concepts for assay analysis. With our expertise in programming and data analysis ^{1,2,5}, our advanced evaluation routines enable a faster and more reliable interpretation of your analysis results and will help optimize your process or product. Our ready-to-use analysis solutions are easily adaptable to your specific needs and provide in-depth mechanistic insight.



References

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