

## Hybrid materials for 3D cell model fabrication

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3D-printed cell models are currently in the spotlight of medical research.<sup>[1]</sup> Whilst significant advances have been made, more realistic models that can mimic the different physical forces and stress factors that cells experience in healthy and pathophysiological conditions are still needed.<sup>[2]</sup> One method to achieve these properties is via hybrid biomaterials, in which inorganic nanoparticles (NPs) and organic materials can be combined to produce a biocompatible and stimuli-responsive environment.<sup>[3,4]</sup> The NPs can provide the physical properties of interest (i.e. optical response, heating, magnetic response, or mechanical strength, etc.), while the organic matrix (polymers, proteins, etc.) can provide the structural microenvironment for cell growth, with controlled porosity or responsiveness toward external stimuli.

In this context, we have been focussed on the synthesis of hybrid inks, composed of plasmonic gold NPs (AuNPs) and functional polymers, which can be printed using high resolution 3D printing techniques. Spatial resolution can be controlled on the micro-scale, allowing multiple different inks to be deposited within proximity. This technique can be used to print human cells combined with the stimuli responsive inks, thereby generating different models of pathological interest. For example, we are interested in generating a model of the arterial wall, composed of 3D printed endothelial and smooth muscle cells. By combining those living inks with a stimuli-responsive hybrid ink, which can contract and expand in response to externally applied light in resonance with the localized surface plasmons of incorporated AuNPs, we aim to simulate the physical changes in the arterial wall. Additionally we are exploring the use of 3D-printed scaffolds containing AuNPs to study tumor growth.<sup>[5]</sup> This model aims to allow the analysis of relevant cancer biomarkers in situ, thanks to the sensing properties of the AuNPs which can be used as Surface Enhanced Raman Scattering (SERS) substrates for Raman-active molecules.

These sophisticated models not only require improvements in cell engineering techniques and in the development of new hybrid materials, but also advanced imaging tools to accurately characterize them.<sup>[6]</sup> As such, we are exploring methods to improve imaging resolution and speed, taking advantage of the inherent NPs of each model to act as contrast agents for correlative imaging techniques.<sup>[7]</sup>

All these aspects will be highlighted to discuss how our advanced hybrid materials could be used in biomedical applications and the advantages they offer over current materials and techniques.

### References

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