

Super resolution microscopy as a tool for tackling nanomedicine challenges

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Our group uses advanced microscopy techniques to visualize and track in living cells and tissues self-assembled nanomaterials with therapeutic potential. The understanding of materials-cell interactions is crucial towards the development of novel nanotechnology-based therapies for treatment of cancer and infectious diseases.

Many biological structures are made of multiple components that self-organize into complex architectures. Here we want to mimic this phenomenon to develop novel bioactive materials such as nanoparticles or nanofibers able to build themselves (1D or 3D self-assembled nanomaterials). Having the self-assembly motif decorated with different functionalities allows a modular and tunable approach that eases sample preparation.[1]

To study the behavior of such complex nanomaterials in action we make use of a variety of optical microscopy techniques, in particular super resolution microscopy (SRM).[2,3] SRM can achieve a resolution down to 20 nm and represents an ideal tool to visualize nanosized objects in the biological environment. In particular we demonstrate how STORM (Stochastic Optical Reconstruction Microscopy) can be used to image a wide range of nanomaterials beyond the diffraction limit: nanoparticles[4], BTA fibers[5], peptidic nanostructures [6], etc.

Remarkably, STORM allows this observation in the biological environment, thus we are able to follow the journey of nanomaterials inside the body: from protein corona formation[7] to extravasation, targeting and tracking nanomaterials inside the cell.[8-10]

References

- [1] Casellas, N.M., Pujals, S., Bochicchio, D., Pavan, G.M., Torres, T., Albertazzi, L., García-Iglesias, M. *Chem. Comm.*, 54(33) (2018) 4112-4115.
- [2] Pujals S, Albertazzi L. Super-resolution Microscopy for Nanomedicine Research. *ACS Nano*. 2019 Aug 19. doi: 10.1021/acsnano.9b05289.
- [3] Pujals, S., Feiner-Gracia, N., Delcanale, P., Voets, I., Albertazzi, L., Super-resolution microscopy: a powerful tool to unveil complex synthetic molecular systems, *Nat. Rev. Chem.* 3, 68–84 (2019).
- [4] Delcanale P, Miret-Ontiveros B, Arista-Romero M, Pujals S, Albertazzi L. *ACS Nano.*, 12(8) (2018) 7629-7637.
- [5] Albertazzi L, van der Zwaag D, Leenders CM, Fitzner R, van der Hofstad RW, Meijer EW. *Science* 344(6183), (2014) 491-5.
- [6] Pujals, S., Tao, K., Terradellas, A., Gazit E., Albertazzi L. *Chem Commun (Camb)*. 53(53), (2017) 7294-7297.
- [7] Feiner-Gracia, N., Beck, M., Pujals, S., Tosi, S., Mandal, T., Buske, C., Linden, M., Albertazzi, L. *Small*, 13(41) (2017) 1701631.
- [8] Feiner-Gracia, N., Buzhor, M., Fuentes, E., Pujals, S., Amir, R.J., Albertazzi, L. *J. Am. Chem. Soc.*, 22;139(46) (2017) 16677-16687.
- [9] Liu, Y., Pujals, S., Stals, P. J. M., Paulöhr, T., Presolski, S.I., Meijer, E.W., Albertazzi, L., Palmans, A. R. A. *J. Am. Chem. Soc.* 140(9) (2018) 3423-3433.
- [10] van Elstrand, D., Pujals, S., Bakkum, T., Bos, E., Oikonomias-Koppas, N., Berlin, I., Neeffjes, J., Meijer, A.H., Koster, A.J., Albertazzi, L., van Kasteren, S.I. *Chembiochem* 19 (2018) 1766-1770.