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Nanoparticle-Based Matrixes for Imaging Mass Spectrometry: Visualization of Drugs Distribution in Solid Tumor Tissues

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Extended Abstract

Drugs imaging is pivotal in oncology where the achievement of a homogeneous drug distribution within tumor tissue is thought to play a crucial role in response to therapy. The use of nanoparticles (NPs) as matrixes in MALDI-MS (Matrix-assisted laser desorption/ionization mass spectrometry) imaging has opened up new opportunities thanks to the almost complete absence of background signals from matrix degradation. Among nanoparticles, inorganic ones characterized by high photo-adsorption, low heat capacity and large surface area, can assure rapid heating, highly localized and uniform energy deposition, affording efficient sample desorption and ionization.

Here, in this context, different inorganic nanomaterials (titania, gold, carbon nanotubes, halloysite) were studied and compared as matrixes in the development of MALDI supports for the ionization of several anticancer drugs (Paclitaxel, Ortataxel, Trabectedin, Imatinib, Lucitanib and Doxorubicin) to study their tumor distribution in xenografts with high resolution and sensitivity.

After a complete physico-chemical characterization, different matrixes were screened by depositing drugs on MALDI plate, followed by matrix suspension on top, but also spraying the matrix suspension on control and treated xenograft tumors sections (10µm) mounted on a MALDI plate and spotted with different drug standards. Finally, the efficiency of different nanostructured matrixes was evaluated spotting the same concentration of five anticancer drugs on MALDI plate, on control tumor tissues and by spraying them on treated tumors. The results show that TiO_2 nanoparticles and Carbon nanotubes (tested on plate in negative ion mode) efficiently ionize and fragment Paclitaxel in the ion source, to produce ions at m/z 284.2 as base peak, corresponding to the side chain with the amide-acyl group. Particularly, P25 TiO_2-NPs based matrix seems to be the best one to visualize Paclitaxel distribution in treated tumor tissues with high sensitivity. Halloysite matrix gives the worst results in both negative and positive ion mode with all drugs spotted on MALDI plate and giving a strong signal suppression when sprayed on tissues with the airbrush. The gold based matrix allows to ionize almost all tested drugs in positive ion mode both on steel MALDI plate and on control tissues spotted with drug standards. In particular, it gives the best results for the ionization of the tyrosine-kinase inhibitors Imatinib, with the dominant ion peak at

515 m/z, and Lucitanib, with the dominant ion at 465 m/z corresponding to the adducts of the molecules with sodium. Furthermore, gold nanoparticles allow the visualization of Imatinib distribution inside the mesothelioma xenograft MPM-487, highlighting that this drug has a peripheral localization in the tumor.

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