A nanostructured matrices assessement to study drugs distribution in solid tumor tissues by mass spectrometry imaging

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Introduction

Drugs imaging is pivotal in oncology for the study of drugs distribution. The use of nanoparticles (NPs) as matrices in MALDI imaging has opened new opportunities thanks to the almost complete absence of background signals from matrix degradation. The use of inorganic fine particles is based on their physical properties like high photo-adsorption, low heat capacity and large surface area. This ensures rapid heating, highly localized and uniform energy deposition, resulting in efficient sample desorption and ionization.
We compared the capability of commercial TiO2 (P25 and Hombikat), gold NPs (GNPs), carbon nanotubes (CNTs) and halloysite nanotubes (HNTs) to ionize anticancer drugs. Objective is to develop specifically designed surfaces to study drugs tumor distribution in xenografts with high resolution and sensitivity.

Methods

Paclitaxel and ortataxel were dissolved in 50% ethanol, trabectedin and lucitanib were dissolved in 50% methanol and doxorubicin was dissolved in H2O at a concentration of 100pmol/µL for all drugs. P25 or Hombikat TiO2, GNPs and HNTs or CNTs matrices were prepared respectively at 1mg/mL, 0.4mM and 0.15mg/mL in 50% ethanol, vortexed and sonicated before use.
The different matrices were screened by depositing 1µL of drugs 100 pmol/µL on MALDI plates waiting until it was dried, followed by 1µL of matrix suspension on top. Matrices efficiency was also tested by spraying the suspension on control and treated xenograft tumors sections (10µm) mounted on a MALDI plate, spotted with different drug standards. The MS used was an AB MALDI-TOF/TOF 4800 series.

Preliminary Data

We directly compared the efficiency of different nanostructured matrices by spotting the same concentration of five anticancer drugs on MALDI plate, on control tumor tissues and by spraying them on treated tumors.
TiO2 nanoparticles and CNTs tested on plate in negative ion mode, efficiently ionizes and fragments paclitaxel in the ion source, to produce ions at m/z 284 as base peak, corresponding to the side chain with the amide-acyl group. Particularly, P25 TiO2-NPs based matrix appears to be the best 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 causes 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 m/z 515, and lucitanib with the dominant ion at m/z 465 corresponding to the sodium adduct. Furthermore, gold nanoparticles allow the visualization of imatinib distribution inside mesothelioma xenograft (MPM-487), highlighting the peripheral localization of this drug.

Novel Aspect

The comparison of different nanostructured matrices allows identification of the best to

visualize anticancer drugs distribution in tumors with MALDI-MSI.