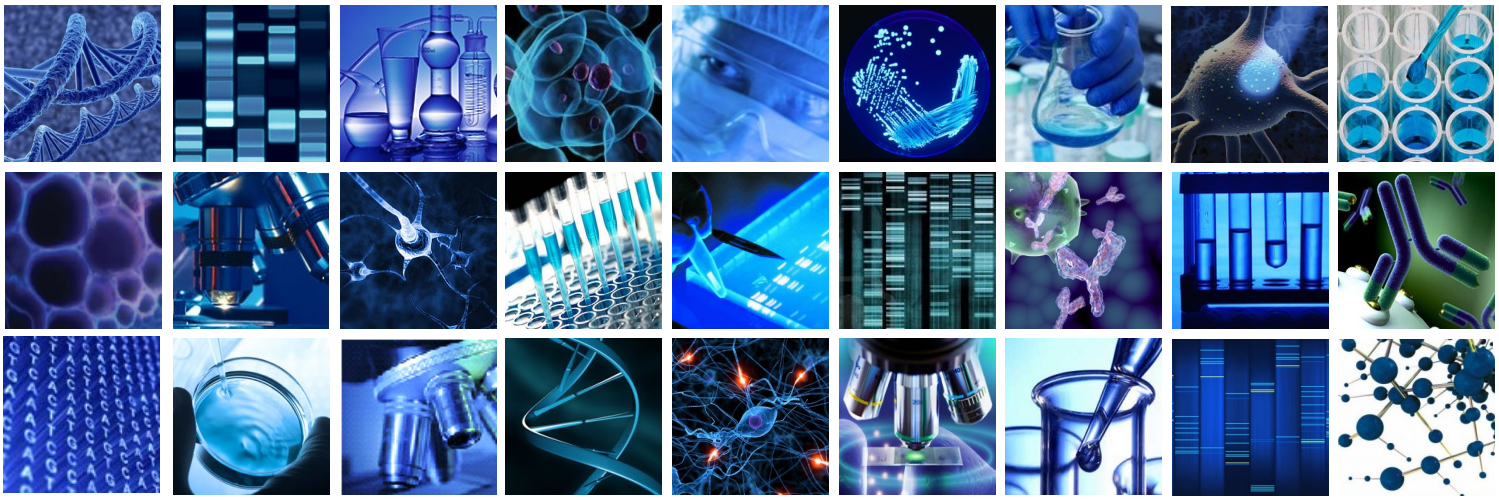

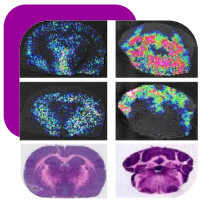

MALDI Imaging Mass Spectrometry and correlation with PK data

Aim of the study

Ex vivo drug detection in tissue sections by MALDI TOF-TOF and MALDI Imaging Mass Spectrometry and correlation with Pharmacokinetic (PK) data in order to investigate and verify the drug accumulation in organs.

Analyte

Small molecule therapeutic candidate (compound A) and its modified analogue (compound B).

Methodology

MALDI imaging mass spectrometry (MALDI-IMS) is a new technology that allows for simultaneous mapping of small molecules (drugs and peptides) and proteins present in thin tissue sections with a lateral resolution of approximately 30–50 µm. Matrix is first uniformly deposited over the surface of the section, utilizing procedures optimized to minimize analyte migration. Molecules are then desorbed from discrete spots or pixels upon irradiation of the sample in an ordered array or raster of the surface. Each pixel thus is keyed to a full mass spectrum consisting of signals from protonated species of molecules desorbed from that tissue region. A plot of the intensity of any one signal produces a map of the relative amount of that compound over the entire imaged surface.

PK analysis for a preclinical study of compounds of interest was previously performed in our laboratory through LC-MS/MS detection and quantitation on plasma.

System murine organs

Therapeutic area Oncology

Development stage Preclinical

Customer a leader company in biotech. Its activity fields are R&D of innovative small molecules and biopharmaceuticals.

Results

PK profiles achieved from the previous bioanalytical analysis performed in our laboratory from through LC-MS/MS, suggested a “reservoir effect”, with the accumulation of the compound B in some organs, followed by a slow release of the compound A due to an enzymatic conversion of the compound B.

MALDI-TOF MS was used to evaluate the presence of both compounds in the organs (kidney, lung and liver) explanted from the same animals. In mice sacrificed 2 hours after administration, Compound A was exclusively found in kidneys, while Compound E was highly present in lungs. None of them was found either in the liver at 2 and 6 hours after administration.

MALDI Imaging MS analysis of lungs, explanted from mice sacrificed 2h after treatment with Compound B, confirmed and allowed to visualize its accumulation into the pulmonary parenchyma, supporting the suggested “reservoir effect”.

Advantage of the methodology

MALDI Imaging technology provides a powerful tool for the investigation of biodistribution because it allows to detect the drug directly on tissue without need to be labeled. The use of MALDI-IMS technique in the drug discovery and development fields is being recognized by important companies working on pharma and has already been successfully used to detect and map pharmaceutical compounds with semi-quantitative analysis by direct MALDI MS analysis of sections from dosed tissues have also been described.

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