From MALDI-IMS lipidomic data to study cell signaling pathways: the importance of the lateral resolution

Gwendolyn Barceló-Coblijn
Institut d'Investigació Sanitària Illes Balears (IdISBa, Balearic Islands Health Research Institute), Palma, Spain

INTRODUCTION

These are definitively exciting times for membrane lipid researchers. Considered for a long time as simple membrane building blocks, the important role these lipids play in cell physiology is steadily being acknowledged. Currently, it is possible to establish the precise lipid composition in a wide variety of biological contexts thanks to the advances in mass spectrometry techniques (MS). However, to fully understand the biological function of each lipid species, we need to know its spatial distribution within the tissue. In the last ten years, the MS field has experienced a profound revolution thanks to the development of imaging MS-based techniques (IMS). In its short lifetime, IMS has proven to be a powerful technique to unravel changes in cell and tissue homeostasis in the context of a disease, but also to understand the role that lipids and proteins play, even in the different cell types present in a given tissue. However, the information that can be withdrawn depends very much on the lateral resolution used during the analysis. Among the several desorption techniques used for IMS, MALDI (matrix-assisted laser desorption/ionization) offers a good compromise between sensibility and lateral resolution.

METHODS

Using MALDI-IMS to analyze human colon mucosa sections, we have demonstrated not only that the lipidome is cell-type specific but also that it is highly sensitive to any change in the pathophysiological state of the cell. Human colon mucosa consists of a single monolayer of colonocytes that invaginates into the stroma, generating the functional units called crypts. At the bottom of these structures reside the adult stem cells that divide and differentiate into fully mature colonocytes while ascending along the crypt. Thanks to the lateral resolution achieved during the IMS analyses (10 µm/pixel), it is possible to follow, pixel by pixel, the changes occurring in the lipidome along the colon crypt.

RESULTS

These analyses revealed how precisely a very specific set of lipids changes along the colon crypt. Impressively, this variation fits a mathematical equation: lipids containing monounsaturated fatty acids increase according to a first-degree equation ($y=ax+b$, $R2=0.95\text{-}0.98$) from the bottom to the top of the crypt, while those containing arachidonic acid decrease according to a logarithmic equation ($y=-\ln(x)+b$, $R2=0.95\text{-}0.98$). Furthermore, using this resolution and based merely on the lipidome, we were able to identify the colonocytes nuclei.

CONCLUSION

While these techniques will help to place membrane lipids in the position they deserve, they also open the black box containing all the unknown regulatory mechanisms accounting for such tailored lipid composition. Currently, we are investigating the changes in gene expression occurring during colonocyte differentiation using a gene expression array (Human Clariom S Pico, Thermo Fisher Scientific). The preliminary analysis of the results reveals a gradual expression of enzymes involved in prostaglandin metabolism along the crypt. Altogether, these results indicate a complex interaction between membrane lipids and prostaglandin metabolism in colonocyte differentiation and tumorigenesis.