INNOVATION WORKSTM





Technology from the European Molecular Biology Laboratory

LiMA: a liposome microarray to systematically study protein-lipid interactions EMBLEM Ref. 707

Challenge

- interaction of proteins with lipids id of fundamental importance in most cellular processes
- limitations in current technologies are the small number of lipids processed per experiment and the lack of stability of artificial surrogate membranes

Commercial Opportunity

- clear market for off-the-shelf or customized LiMA chips and screening service
- licensing and full transfer of the technology to a licensee

Technology

- microarray chip to measure protein recruitment to membranes
- coupled to high-throughput fluorescence microscopy for data collection
- · single lipids or lipid combinations can be screened
- multiplexing of lipids and/or proteins is possible
- the microarray chips can be stored for at least two months, uncoupling the steps of production and experiment
- measurements are conducted in a physiological environment
- LiMA can be adapted to additional downstream analyses such as mass spectrometry

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Key Inventors

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Intellectual Property

GB1212896.3, filed 20.07.2012 PCT/EP2013/065256, filed19.07.2013





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Considering that a eukaryotic cell produces more than 1000 different lipid species, each with distinct properties and often acting in combination, a tool is needed that enables the study of protein-lipid interaction in a manner that is on par with the functional genomics resources now available, i.e. a simple device to comprehensively study protein-lipid interaction in a physiological, sensitive, reproducible, cooperative and high-throughput manner. LiMA is such a device and we have to date successfully used it with more than 130 single different lipids including all the main classes (glycerolipids,

phosphatidylinositol phosphates, sphingolipids, sterols) and a plethora of combinations, on a wide variety of proteins. In a large-scale study we systematically tested the interaction of more than 90 proteins with a variety of liposome compositions in over 10.000 single assays. LiMA is a microarray chip designed to measure protein recruitment to membranes. Single lipids or lipid combinations are spotted, together with a carrier lipid on a thin agarose layer. LiMA chips can the be dried and stored under argon for at least 2 months. Before se they are hydrated with a buffer of choice. Giant, unilaminar liposomes, i.e. surrogates of biological membranes, form within 2 mins and stay stable in size, shape and location for at least 6 hrs. LiMA produces liposomes of virtually any composition and size, in a physiological environment. LiMA is amenable to high-throughput microscopy and its fabrication and handling is simple, as is the scale-up. LiMA significantly reduced the amount of lipid and protein needed as it is highly sensitive and interactions with less than 1pmol protein can be measured. It is also quantitati've because binding intensities are proportional to the amount of lipid and protein given lipid-protein pair. It also captures cooperative binding mechanisms.

LiMA is capable of identifying discrete changes in binding affinities in response to mutation or drug interference.

References

Saliba et al. 2014, Nat Methods doi: 10.1038/nmeth.2734

Vonkova et al. 2015, Cell Rep doi: 10.1016/j.celrep.2015.07.054

