Lipid Arrays

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The "Omics revolution" has led to the recent emergence of "lipidomics"[1], a field dedicated to the study of lipids and how they interact with proteins and other cellular components. By identifying lipid-associated molecules in a cell or biological fluid, lipid microarrays are a useful tool for increasing the knowledge base of the human lipidome[1,2]. Much like antibody and other protein microarrays, lipid arrays are protein-detecting microarrays. Lipid microarrays consist of various lipid sub-types spotted individually, in an array pattern, on a solid surface. The lipid array provides a protein-lipid interaction profile and can be used to identify proteins of potential therapeutic value[2]. Protein overlay lipid blots (colloquially termed "Fat Westerns") have previously been used for biochemical investigations on lipid selectivity[1,3] and could be considered a precursor of lipid microarrays. The main advantage of lipid arrays over protein overlay lipid blots is the ability for lipid arrays to simultaneously assess the protein-lipid interaction between hundreds of arrayed lipids and a complex mixture of proteins from a biological sample. In addition, lipid arrays are simple, chemiluminescence-based assays and array production can be automated[4].

Lipids form many structural features of cells and are critical members of cellular signal transduction pathways[2]. They are also important targets of immune responses in several microbial and autoimmune diseases[4]. For example, autoimmune responses directed against phospholipids and gangliosides contribute to the pathogenesis of systemic lupus erythematosus and Guillain-Barre syndrome, respectively[5]. Lipid microarrays have recently been used to investigate the hypothesis that myelin lipids may be target autoantigens in individuals with multiple sclerosis (MS)[4]. Kanter *et al.* generated lipid microarrays comprised of the lipid sub-types found in the myelin sheath and evaluated samples from MS and control patients using these arrays[4]. Based on the results, Kanter *et al.* were able to detect lipid-specific antibodies against sulfatide, sphingomyelin and oxidized lipids in cerebrospinal fluid from MS patients[4].

The manufacture of lipid microarrays involves some challenges. Modified lipids can be immobilised to functionalised solid surfaces, such as epoxy and carbonyl diimidazole, by covalent attachment. Despite being a laborious process, chemical modification of the lipids doesn't usually affect their functionality as most lipid molecules have long fatty acid chains that can be used for chemical derivatisation[6]. Due to their amphiphilic nature, lipids can also be immobilised non-covalently to hydrophobic solid surfaces or porous surfaces. For example, polyvinylidene fluoride (PVDF) membranes attached to microscope slides have been used for arraying lipid solutions[4]. It is believed that the hydrophobic part of the lipid anchors the lipid to the hydrophobic PVDF array surface, thus the lipid molecules are oriented such that the polar regions, such as the sulfate group or glycan molecule, are accessible for protein binding[4]. The advantages of non-covalent immobilisation for lipid array production include: derivatisation of the ligand molecule is not required, porous substrates may permit the immobilization of a larger amount of probe molecules, and porous substrates may provide a 3-D hydrophilic environment similar to solution phase for biomolecular interactions to occur[1]. The difficulty of producing high-concentrate lipid solutions for use in conventional pin or ink-jet spotters has provided the impetus to develop a polydimethyl siloxane (PDMS) flow spotter for the patterning of lipid microarrays[2]. By forming lipid spots through continuous flow, high-density arrays can be made with more dilute lipid solutions. In addition, flow deposition offers improved spot formation and allows spots of different concentrations to be printed, since flow rates and deposition times could be uniquely varied for each spot.

Since many lipids do not exist in isolated form but rather aggregate in bilayers and membranes, it is likely that lipid bilayer and cell membrane arrays may gain popularity in the future. Simon *et al*. have published a paper about the formation and stability of a suspended biomimetic lipid bilayer on silicon submicrometer-sized pores[7]. This study discusses progress in lipid bilayer printing using the Langmuir-Blodgett (LB) technique, a method used to create a molecular film of surfactant at the air-water interface[8]. This technique allows for the preparation of ultrathin layers suitable for lipid immobilisation and protein-lipid interaction studies[9]. In addition, cell membrane microarrays have also emerged as a tool that facilitates the study of ligand-receptor interactions and cell-cell signalling[10]. Cell membrane arrays consist of lipid bilayers containing biological molecules of interest supported on a solid substrated[10].

References

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