

S6\_O-01

## Hierarchy of interactions dictating the thermodynamics of cell membrane lipid bilayers: a calorimetric route

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**Keywords:** model membranes, DSC, free fatty acids, type 2 diabetes mellitus

Cells and vesicles functionalities, as well as membrane proteins one, are strictly correlated to membrane lipid composition because of its influence on membrane thermodynamic stability [1]. In this frame, a stepwise study of vesicles with different morphology and lipid composition was performed through high-sensitivity differential scanning calorimetry at physiological pH with the purpose of comprehending the role played by some of the main factors that contribute to the thermodynamic stability of cell membranes. The phospholipid bilayer of Insulin Secretory Granules (ISGs), vesicles located in the pancreatic Langerhans  $\beta$ -cells and which are responsible for insulin and amylin storage and secretion in response to nutrient intake, was considered as reference system.

The cross-study of single-component and binary systems composed by different phospholipids allowed the dissection of the roles played by curvature, phospholipid headgroups and tails on the thermotropic behaviour of cell membranes [2]. Therefore, a hierarchy of contribution to the overall thermodynamic stability of membranes was depicted as membrane curvature < phospholipid headgroup < phospholipid tail < phospholipid unsaturation. The following inclusion of sphingomyelins and lysophosphatidylcholines together with a more complete fatty acids distribution allowed the achievement of a high-complexity fourteen-components model membrane that reflected the 80% of ISG's phospholipids. The inclusion of cholesterol was finally considered for the achievement of the final ISG-like membrane [3].

Furthermore, the effect of several Free Fatty Acids (FFAs), whose levels are recurrently altered in diabetic and/or obese subjects, on the thermodynamic stability of selected membranes was investigated. The results highlighted strong stabilizing effects on the membranes as well as pronounced phase segregations in the case of saturated acids, moderate stabilizing effects for a *trans*-unsaturated FFA, whereas opposite effects were observed in the case of *cis*-unsaturated ones [2,3].

### References

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