Testing the membrane pacemaker model of metabolism

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Much of the metabolic chemistry of life occurs in the lipid rich environment of membranes. Although membrane lipid composition is often seen as relatively constant this belies both processes that continuously remodel these structures as well as the differences between species. In a series of comparisons that differ greatly in metabolic rate (namely ectotherms *vs* endotherms, newborn *vs* adult rats, large mammals *vs* small mammals, large birds *vs* small birds) we have observed a correlation with the fatty acid composition of cellular membranes and metabolic rate. Low metabolic rates are associated with monounsaturated (i.e. lipids with fatty acids with only one C=C) and high metabolic rates are associated with polyunsaturated (i.e. lipids with fatty acids with two or more C=C) membranes. In essence there is a link between membrane lipid composition and metabolism; this link forms the basis for the membrane pacemaker theory of metabolism.

Much of our work on the relationship between membrane lipid composition and metabolism has been derived from examining the sodium pump (Na^+K^+-ATPase). Constituting up to 20% of the resting metabolism, the sodium pump in different species has vastly different rates of molecular activity (i.e. rate of substrate turn-over) with higher rates of molecular activity associated with polyunsaturated and lower rates associated with monounsaturated membranes. In order to test these correlations, species membrane lipid cross-over experiments were performed. Basically, sodium pumps from tissues (kidney or brain) of species with high and low sodium pump molecular activities were crossed-over with membrane lipid from the same tissue of each species (namely; rat against toad, cow against crocodile and adult rat against neonate rat). In all cases, the results showed molecular activities shifted in the direction of the added membrane lipid source. Namely, original membrane lipid restored original molecular activity, sodium pumps with high molecular activity when added with lipid from membrane with low sodium pump molecular activities resulted in decreased activity and conversely sodium pumps with low molecular activity when added with lipid from membrane with high sodium pump molecular activities resulted in increased activity. The order of change in some cases was as much as a 2-3 fold increase or decrease in molecular activity. These results clearly suggest that membrane lipid composition may play a significant role in determining the molecular activity of membrane bound proteins such as the sodium pump, and in so doing set the pace of metabolism. One consequence of this possibility is that membrane lipid composition can be influenced by dietary fat intake and that may have significant implications for metabolic based processes.