Submicrometric lipid domain contribution to red blood cell (re)shaping

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Although lipid domains have been evidenced in several living cell plasma membranes, their roles remain largely unclear. We investigated whether they could contribute to function-associated cell (re)shaping. To address this question, we used erythrocytes as cellular model since they (i) exhibit a specific biconcave shape, allowing for reversible deformation in blood circulation, which is lost by membrane vesiculation upon aging; and (ii) display at their outer plasma membrane leaflet two types of submicrometric domains differently enriched in cholesterol and sphingomyelin. We reveal the specific association of cholesterol- and sphingomyelin-enriched domains with distinct curvature areas of the erythrocyte biconcave membrane. Upon erythrocyte deformation, cholesterol-enriched domains gathered in high curvature areas. In contrast, sphingomyelin-enriched domains increased in abundance in RBC concavity, along with secondary calcium efflux, during subsequent shape and volume restoration. Upon erythrocyte storage at 4°C (to mimick aging), lipid domains appeared as specific vesiculation sites. Our data indicate that lipid domains could contribute to erythrocyte function-associated (re)shaping.