

Adsorption-induced Conformational Changes in Plasma Proteins Mediate Platelet Adhesion to Biomaterial Surfaces

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1. Background and objectives

Platelet adhesion mediates hemocompatibility of biomaterials. The currently accepted hypothesis is that this adhesion is primarily driven by the amount of adsorbed protein on a surface. We hypothesize, however, that conformation of the adsorbed plasma protein layer mediates subsequent platelet adhesion.

2. Methods

Gold-coated quartz slides are incubated in alkanethiol solutions to prepare self-assembled monolayer (SAM) surfaces with varying terminal functionalities. SAMs are preadsorbed with human serum albumin and fibrinogen, prior to exposure to a platelet suspension.

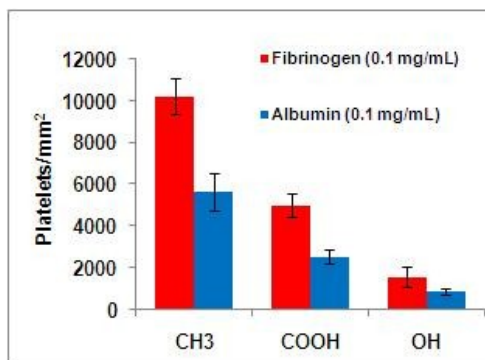
Adsorption-induced conformational changes are assessed using circular dichroism (CD) spectroscopy. Platelet adhesion is measured using a Lactate Dehydrogenase (LDH) assay, and platelet morphology visualized via scanning electron microscopy (SEM).

3. Results

Both proteins exhibited loss of α -helix (and increase in β -sheet) on hydrophobic surfaces, while their adsorbed structures on hydrophilic surfaces were close to native structure. Preliminary platelet adhesion results are consistent with recent studies and show that platelet adhesion correlates strongly with the amount of adsorption-induced denaturation of the adsorbed protein for both fibrinogen and albumin.

4. Discussions and conclusions

Studies have shown significant platelet and macrophage adhesion on hydrophobic surfaces preadsorbed with albumin, although albumin does not contain any known cell-binding domains, suggesting that mechanisms underlying cell interactions with adsorbed proteins maybe different than previously believed. Ongoing studies aim at examining the degree of adsorption-induced conformational change in proteins as a function of surface chemistry and correlating this with platelet response, with the goal of designing hemocompatible cardiovascular biomaterials.



Surface	Fibrinogen (0.1mg/mL)		Albumin (0.1 mg/mL)	
	α -helix (%)	β -sheet (%)	α -helix (%)	β -sheet (%)
Native	40.1 \pm 1.1	9.6 \pm 1.1	63.8 \pm 2.3	2.0 \pm 1.1
OH	41.2 \pm 0.2	9.6 \pm 1.1	52.7 \pm 1.7	2.1 \pm 0.1
COOH	25.7 \pm 1.5	18.8 \pm 1.6	41.5 \pm 0.8	8.0 \pm 2.2
CH3	20.6 \pm 1.7	25.4 \pm 0.7	16.2 \pm 1.6	28.3 \pm 2.3

Platelet adhesion (left) and adsorption-induced conformational changes (right) in fibrinogen and albumin on SAM surfaces. (n=6, Mean \pm 95% CI)

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