An Analysis of the Binding Function and Structural Organization of the Protein Corona

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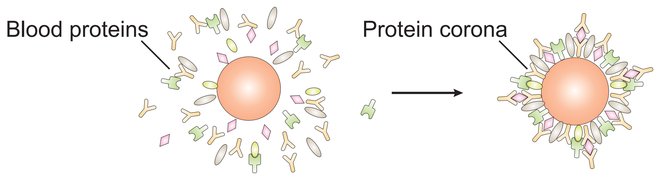
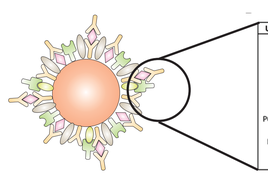
Nanomedicine, when used in the blood, can adsorb proteins on their surface, forming the so-called "Protein corona"

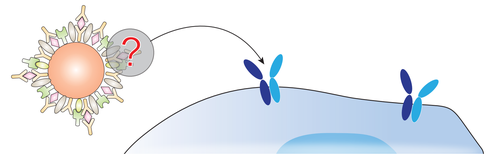


Studies have identified the adsorbed proteins to understand how these proteins affect nanomedicine behaviour in vivo



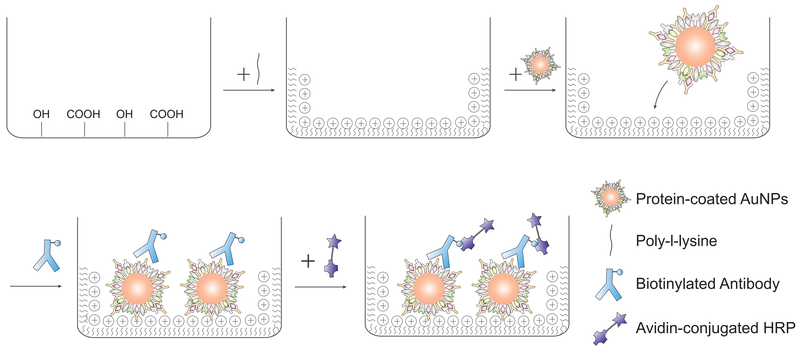
Uniport ID	Protein name	Abbr.	Uniport ID	Protein name	Abbr.
P01024	Complement C3	C3	P01857	Immunoglobulin G	IGG
P01008	Antithrombin-III	ATIII	P02787	Transferrin	TF
P08603	Complement factor H	CFH	P18428	Lipopolysaccharide-binding protein	LBP
P02751	Fibronectin	FN	P68871	Hemoglobin	Hb
P12259	Coagulation factor V	FV	O00602	Ficolin-1	FCN1
P0C0L4	Complement C4	C4	P02656	Apolipoprotein C-III	APOC3
P02776	Platelet factor 4	PF4	P02775	Platelet basic protein	PBP
P02671 (+1)	Fibrinogen	FIB	P03950	Angiogenin	ANG
P03952	Plasma kallikrein	PK	P02766	Transthyretin	PALB
P10909-2	Clusterin	CLU	P03951	Coagulation factor XI	FXI
P01009	Alpha-1-antitrypsin	AAT	P27918	Properdin	CFP
P10720	Platelet factor 4 variant	PF4	P02652	Apolipoprotein A-II	APOA2

But, which of these identified proteins are functional for binding? And what governs its function?

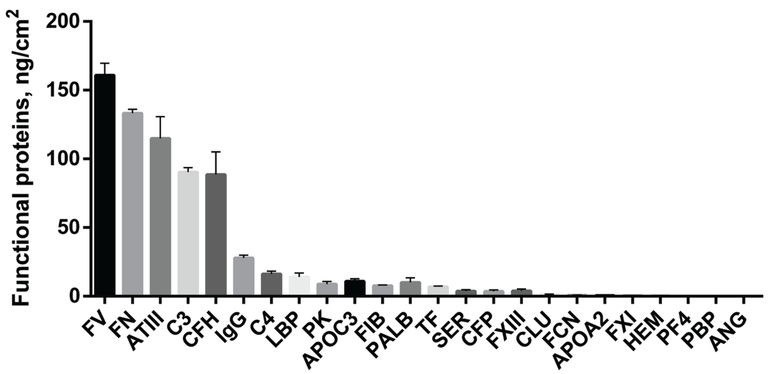


Binding function

Quantify functional proteins nanoparticles using modified ELISA

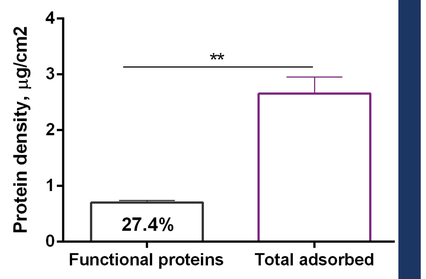


Quantify 24 selected proteins for their functionality in the protein corona



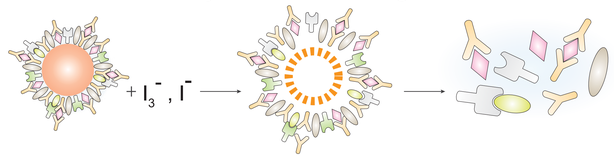
Not all proteins are functional in the protein corona

- These 24 proteins were selected based on their abundance in the corona
- After quantifying the number of functional protein, we found that it only adds up to 27.4% of the total amount that they have on the surface of nanoparticles
- We hypothesized that the structure of how proteins are organized in the corona, resulted such a low number of function protein

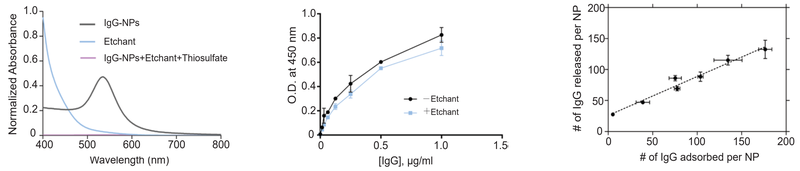


Structural organization

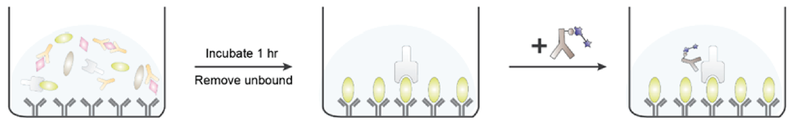
Release the protein corona in their native form to study the structural organization

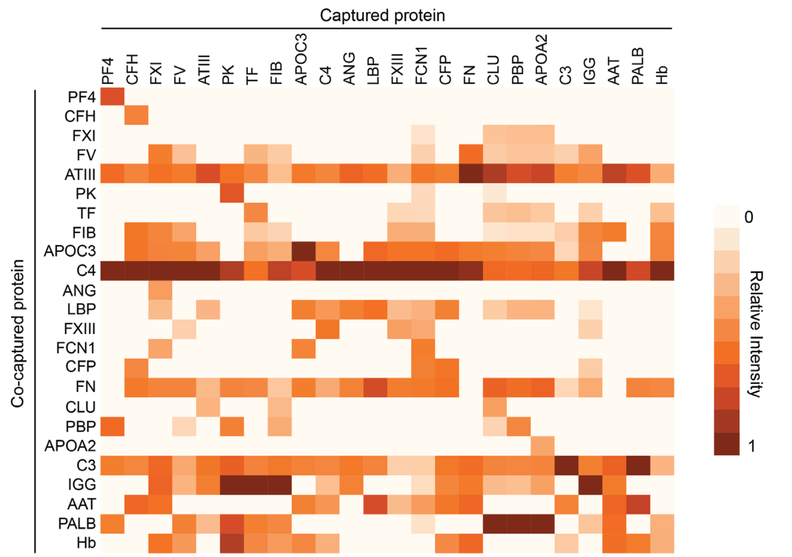


- The nanoparticle core is dissolved
- Proteins remain in their native form
- All released from nanoparticles



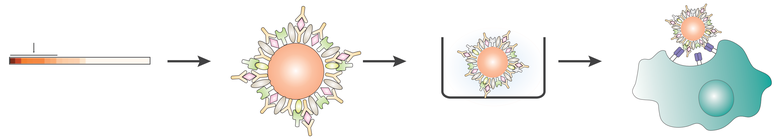
Screen for protein-protein binding pairs that exits in the corona structure





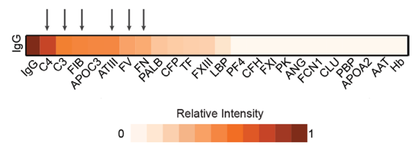
Controlled protein function

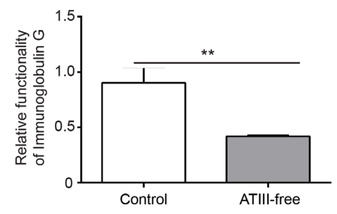
Identify protein binding partners → Deplete from the protein corona → Quantify the binding functionality → Evaluate cellular interactions



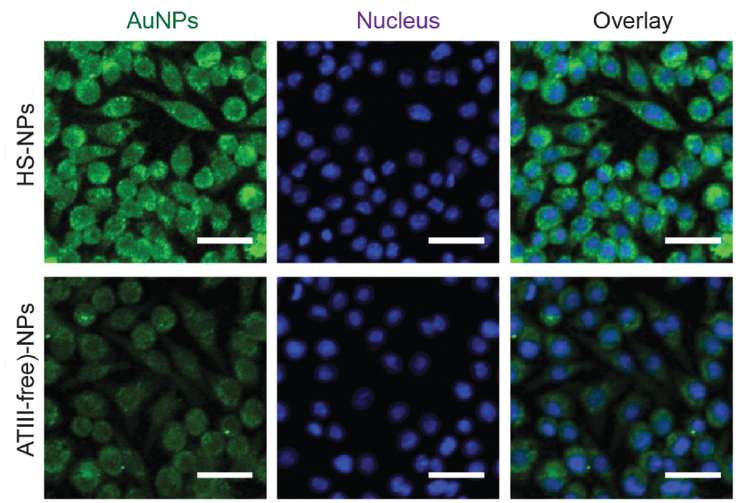
Controlling Immunoglobulin G (IgG) function in the protein corona

- IgG in the protein corona is responsible for the nanoparticle sequestration by macrophages in vivo
- We identified all the binding pair of IgG in the protein corona and depleted them one at a time
- Depleting antithrombin III (ATIII) leads to decreased overall IgG functionality on nanoparticles





Modified protein corona on nanoparticles bind less to macrophages



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