





Complement proteins bind to nanoparticle protein corona and undergo dynamic exchange in vivo

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Association of Blood Proteins with Large Unilamellar Liposomes in Vivo

RELATION TO CIRCULATION LIFETIMES*

(Received for publication, February 20, 1992)

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NANOMEDICINE

Evolution of the nanoparticle corona

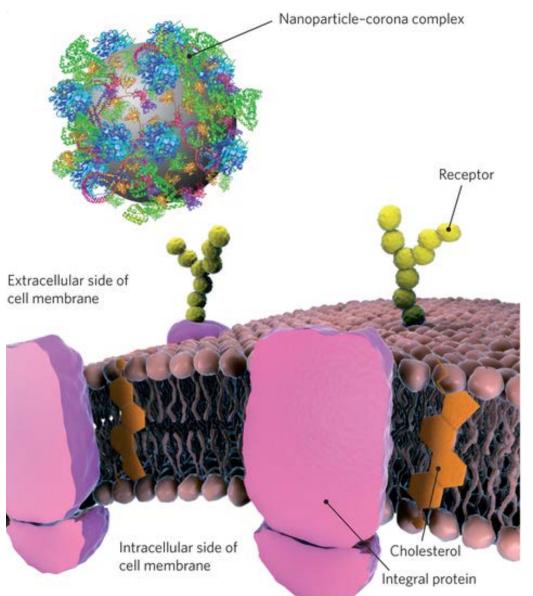
Understanding how complement proteins bind to nanoparticles and participate in their surface 'corona' can provide further insight into the relevance of the protein corona concept in medicine.

Marilena Hadjidemetriou and Kostas Kostarelos

Sources:

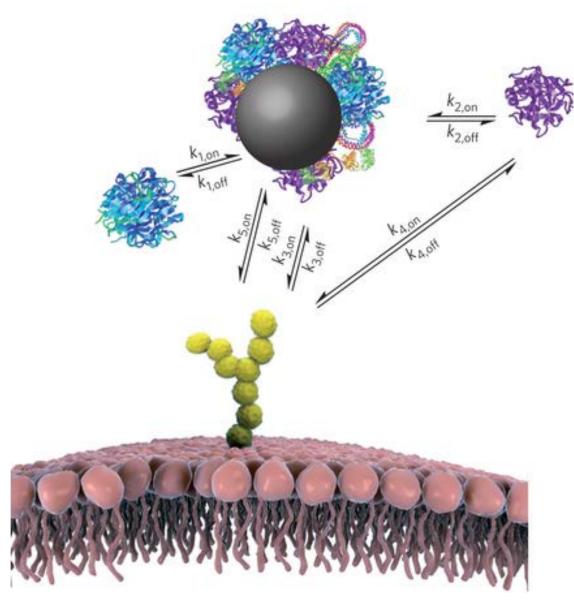
Chen, F. et al. Nat. Nanotech. 12, 387–393 (2017) Hadjidemetriou, M. et al. Nat. Nanotech. 12, 288-290 (2017) Chonn, A. et al. J Biol Chem., 267, 18759-18765 (1992)

The Nanoparticle Corona Concept



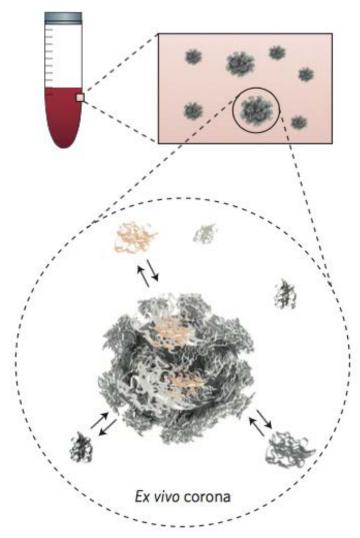
- The 'corona' of biomolecules lowers the surface energy of the nanoparticle and promotes its dispersion
- The nanoparticle-corona complex, rather than the bare nanoparticle, interacts with biological machinery.

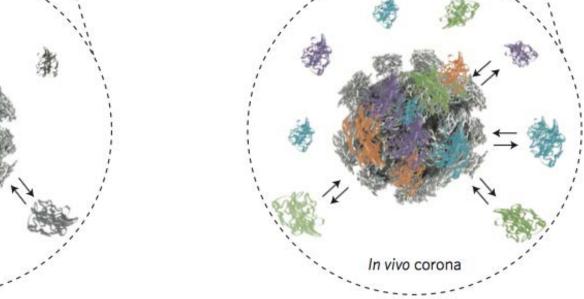
The Biological Identity of a NP



- The corona constitutes a major element of the biological identity of the nanoparticle.
- Soft vs. Hard corona complexes
- The corona around the NPs is kinetically unstable, undergoing constant exchange with the physiological environment.
- Impact on NP targeting

The Biomolecular Corona In Vivo





- **Source:** Hadjidemetriou, M. et al. Nat. Nanotech. 12, 288-290 (2017)
- Static conditions
- Reaches equilibrium

- High flow conditions
- Dynamic exchange
- · Molecularly rich

Evolution of Nanoparticle Corona

1960s 2007 2017

'Protein adsorption'



- Liposomes and polymeric NPs
- Ex vivo and in vivo investigations
- Qualitative characterization
 - Gel electrophoresis
- Pharmacology of NPs
 - Functionalization (PEG dilemma)
 - Opsonization
 - Blood circulation half-life

'Protein corona'



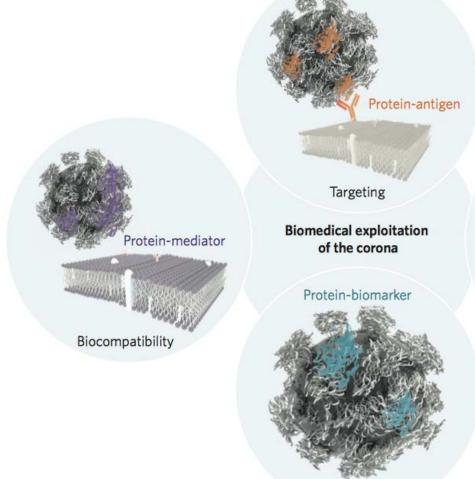
- Lipid, carbon, metal-based NPs
- Ex vivo investigations
- Protein characterization
 - Mass spectrometry
- Biological impact
 - Cytotoxicity
 - Cell internalization
 - Targeting

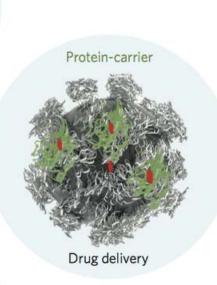
'Biomolecular corona'



- Lipid, carbon, metal-based NPs
- Ex vivo and in vivo investigations
- Molecular characterization
 - Mass spectrometry
 - Genomics
 - Lipidomics
 - Metabolomics
- Biomedical exploitation
 - Targeting
 - Diagnosis
 - Drug delivery etc.

From Obstacle to Engineering Tool?





- Can we exploit the biomolecular corona:
 - o As a means to target specific cells?
 - o To mitigate potential cytotoxicity of NPs
 - o As a "bio-fingerprint" for early disease detection?

Take home

Although the corona is difficult to fully understand, its role in affecting targeting/delivery of nanoparticles is becoming clearer and can potentially be used to further enhance nanoparticle therapy

Discussion Questions

 Can you think of potential implications / applications of nanoparticle corona in the context of cancer?

Discussion Questions

- How important is it to understand hard vs soft corona?
- How can we learn more about the soft corona?



