Transfusionsmedizin

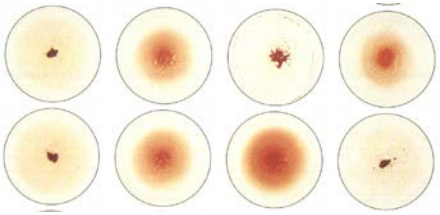
Andreas Greinacher
UMG

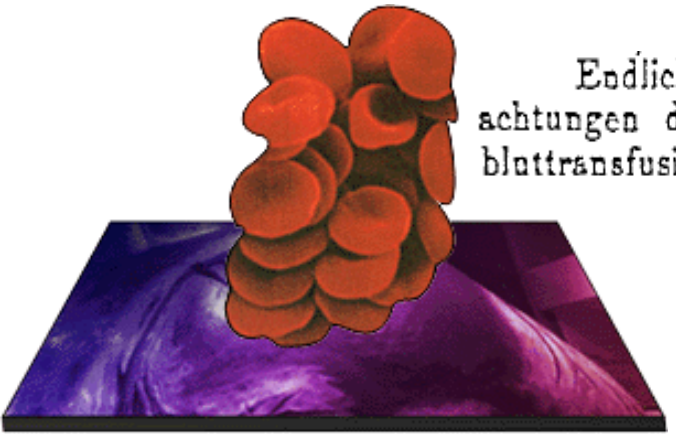
Aus dem pathologisch-anatomischen Institute in Wien.

Ueber Agglutinationserscheinungen normalen menschlichen Blutes.

Von Dr. Karl Landsteiner, Assistenten am pathologisch-anatomischen Institute.

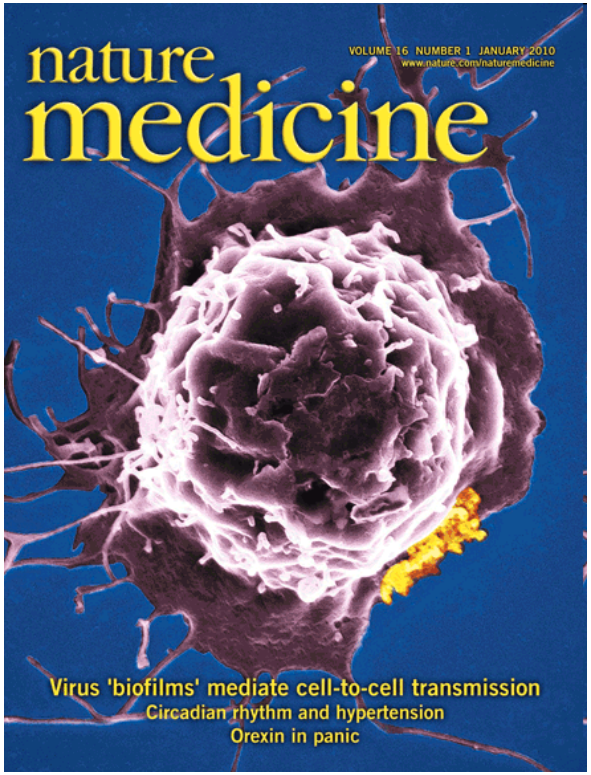
Vor einiger Zeit habe ich beobachtet und mitgetheilt[1]), dass öfters Blutserum von normalen Menschen rothe Blutkörperchen anderer gesunder Individuen zu verklumpen im Stande ist.





Endlich sei noch erwähnt, dass die angeführten Beobachtungen die wechselnden Folgen therapeutischer Menschenbluttransfusionen zu erklären gestatten.

Landsteiner K, Wiener Klinische Wochenschrift 1901;46:132-134

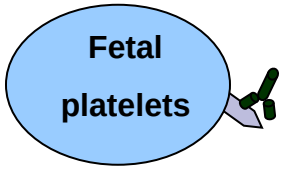


Characterization of the human neutrophil alloantigen-3a

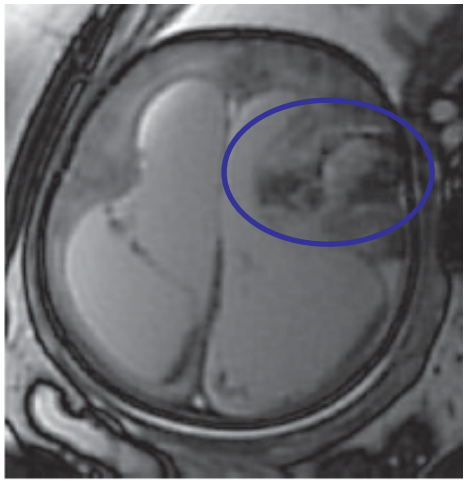
Andreas Greinacher, Jan Wesche, Elke Hammer, Birgitt Fürll, Uwe Völker, Angelika Reil & Jürgen Bux

2010;16:45-8

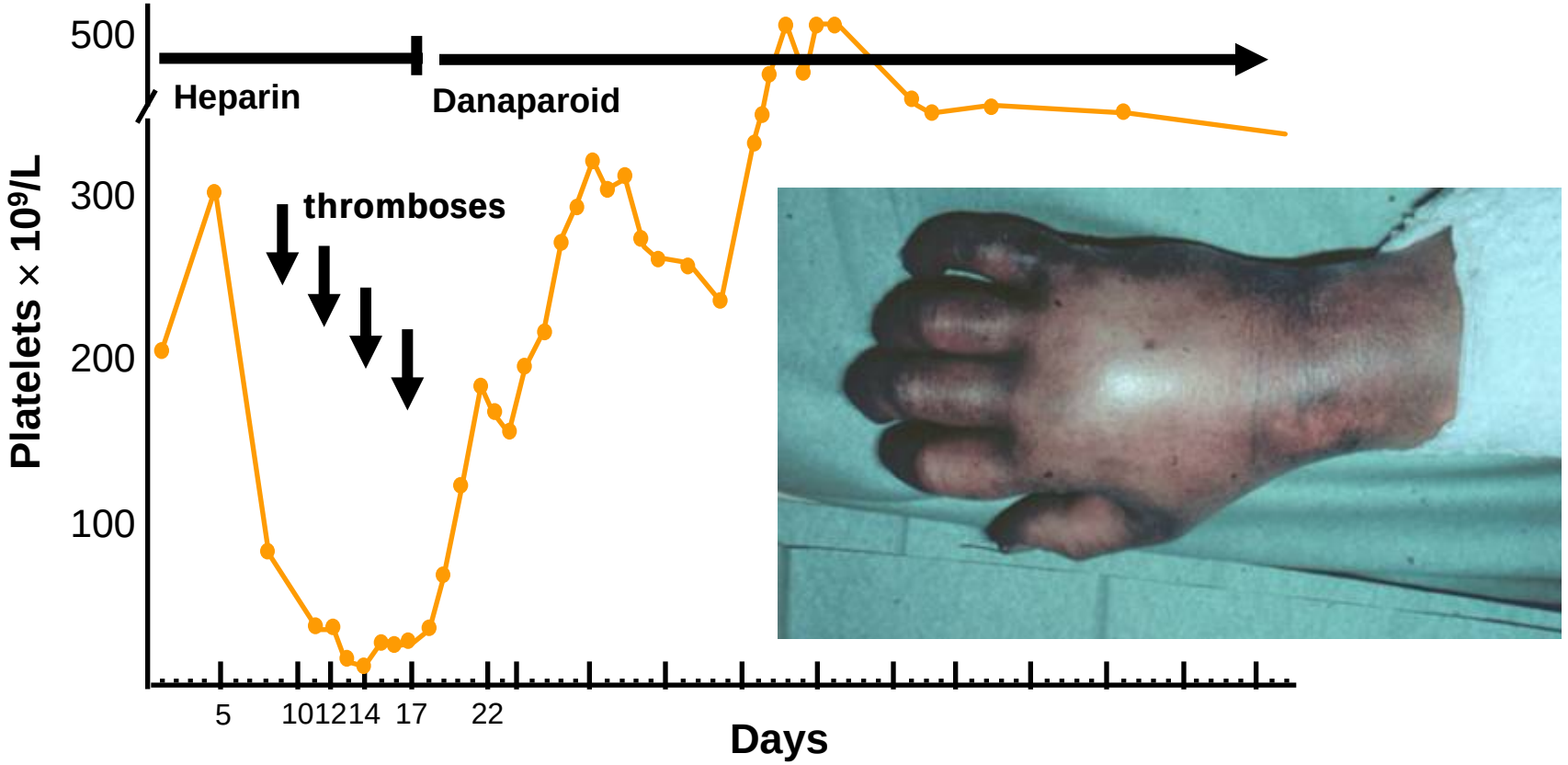
maternal anti-HPA-1a IgG



SZ21



Bovine neonatale Panzytopenie



Greinacher A, et al. *Ann Haematol.* 1992;64:40–42.

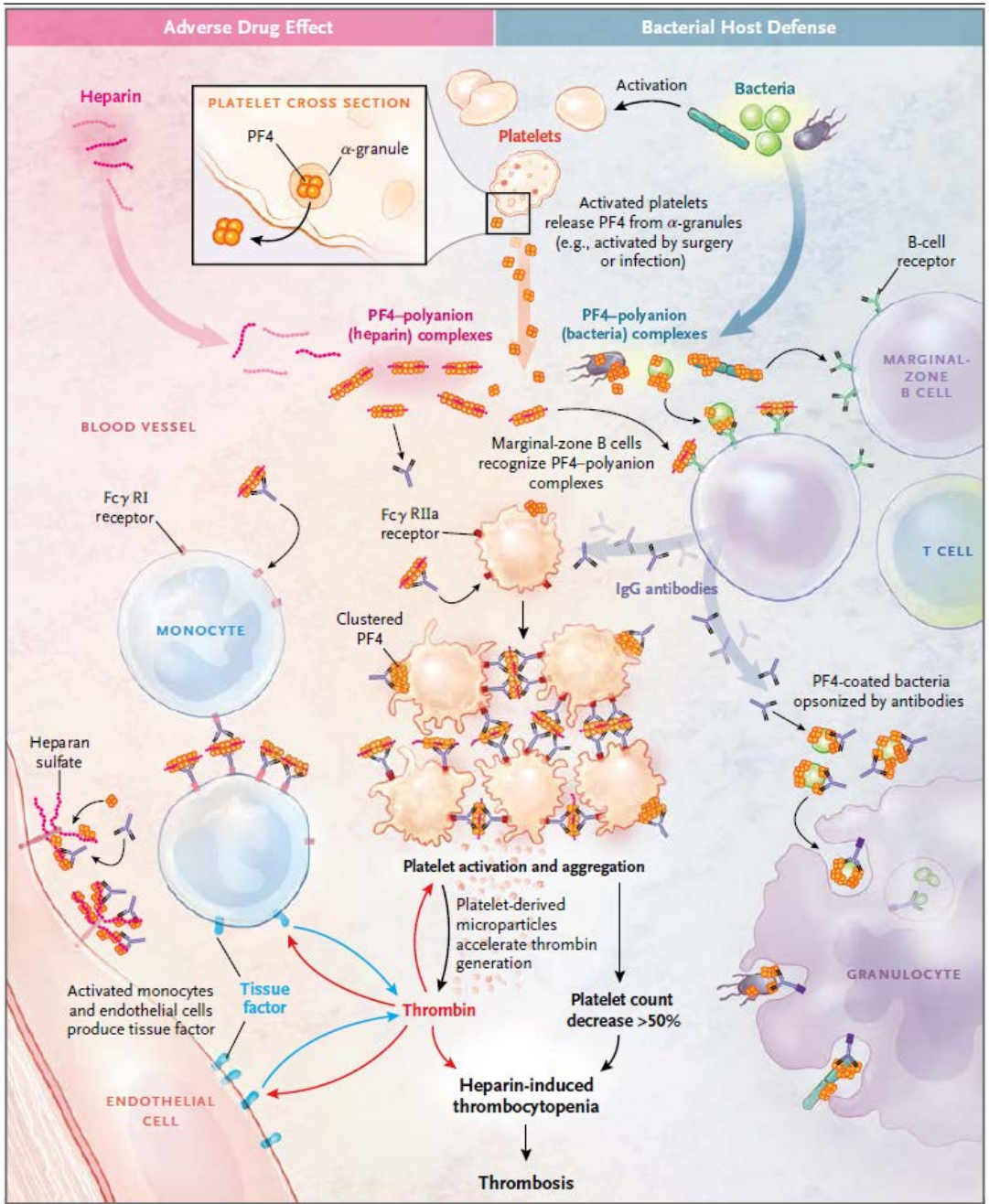


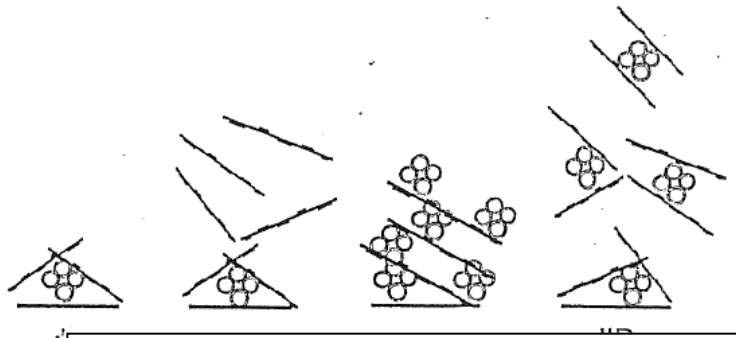
Figure 1. Pathogenesis of Heparin-Induced Thrombocytopenia.

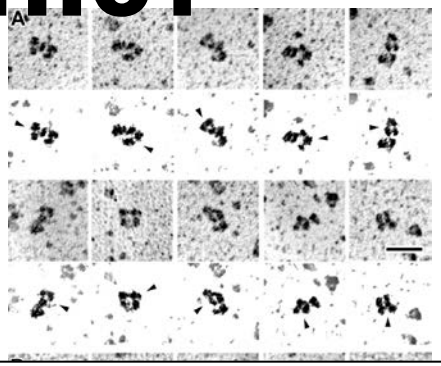
Greinacher A New Engl J Med 2015;373:252-61

Hypothese

- Prokaryonten sind stark negativ geladen
- Eukaryontenzellen sind weniger stark negativ geladen
- Das Immunsystem hat keine Rezeptoren für Ladung
- Moleküle wie PF4 dienen als Marker für negative Ladung

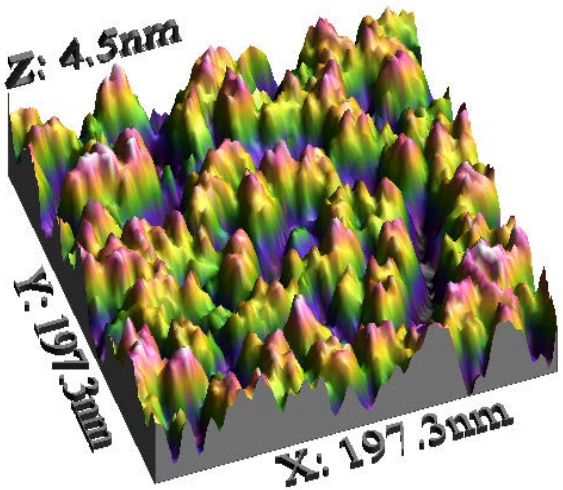
Why becomes PF4 immunogenic?



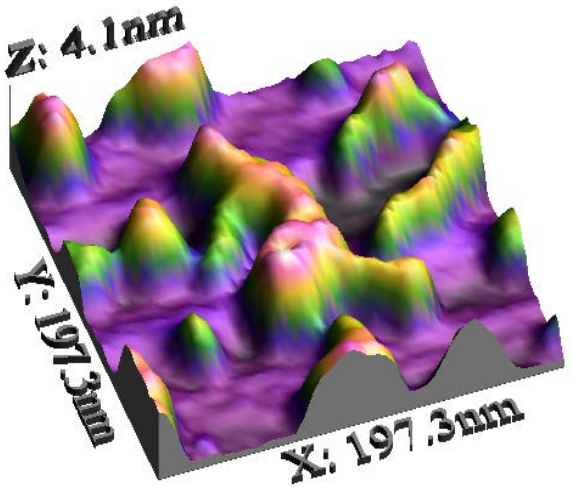


Clustering or conformational change and expression of a neoepitope?

Grei 8

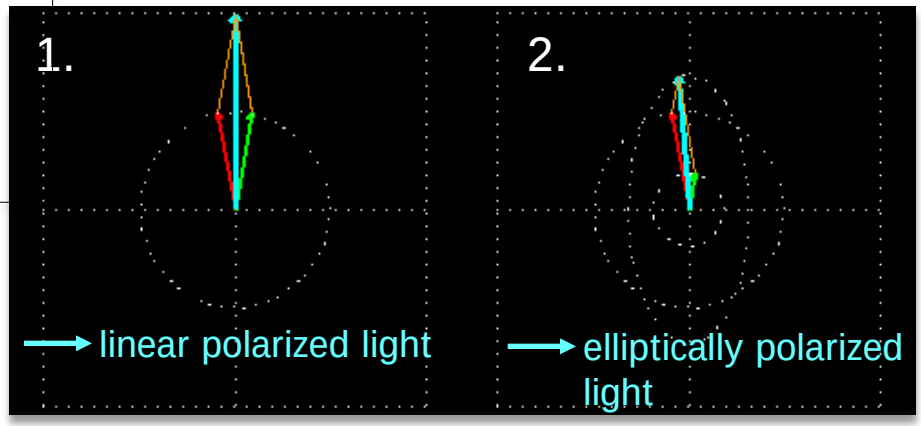


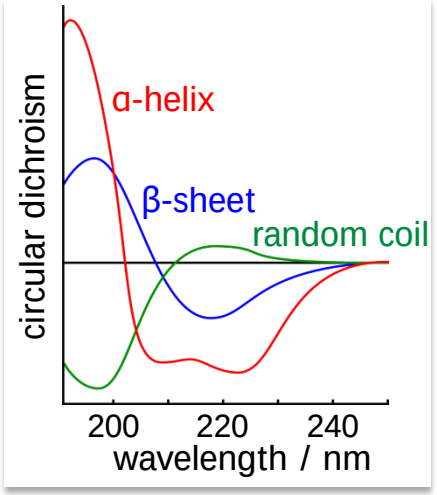
+ heparin

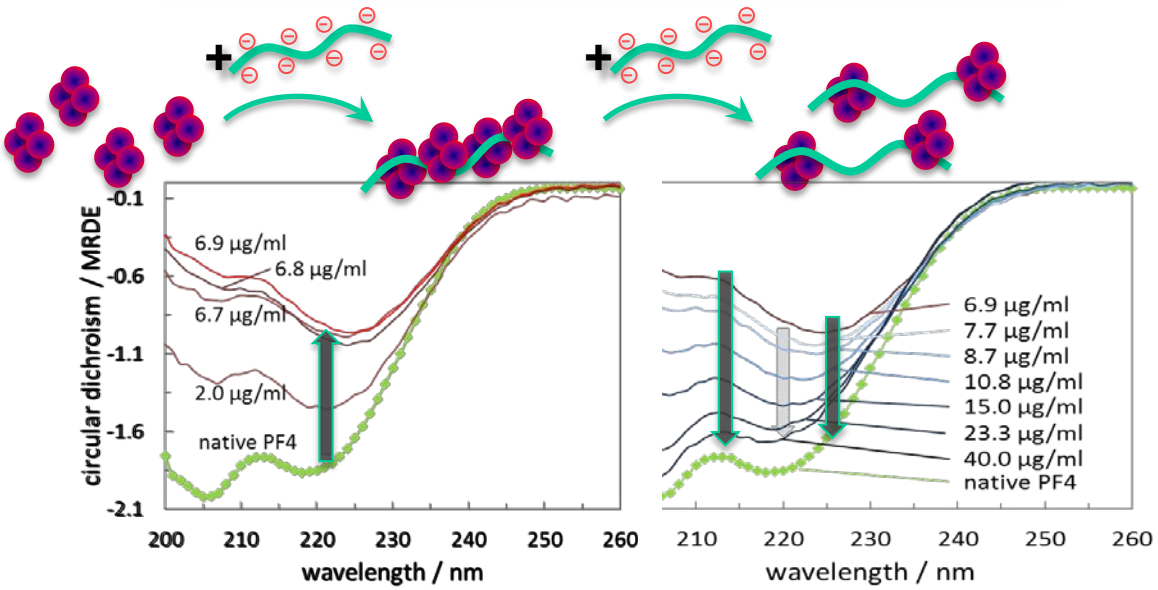


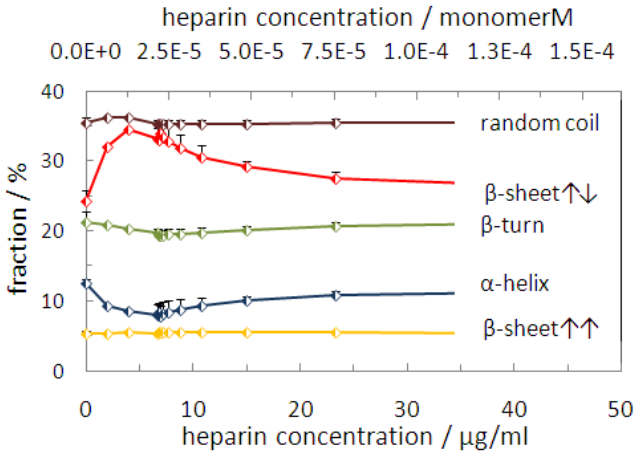
Greinacher A. et al. ATVB 2006;26:2386-93

Investigating the secondary structures of PF4: Circular Dichroism (CD) Spectroscopy





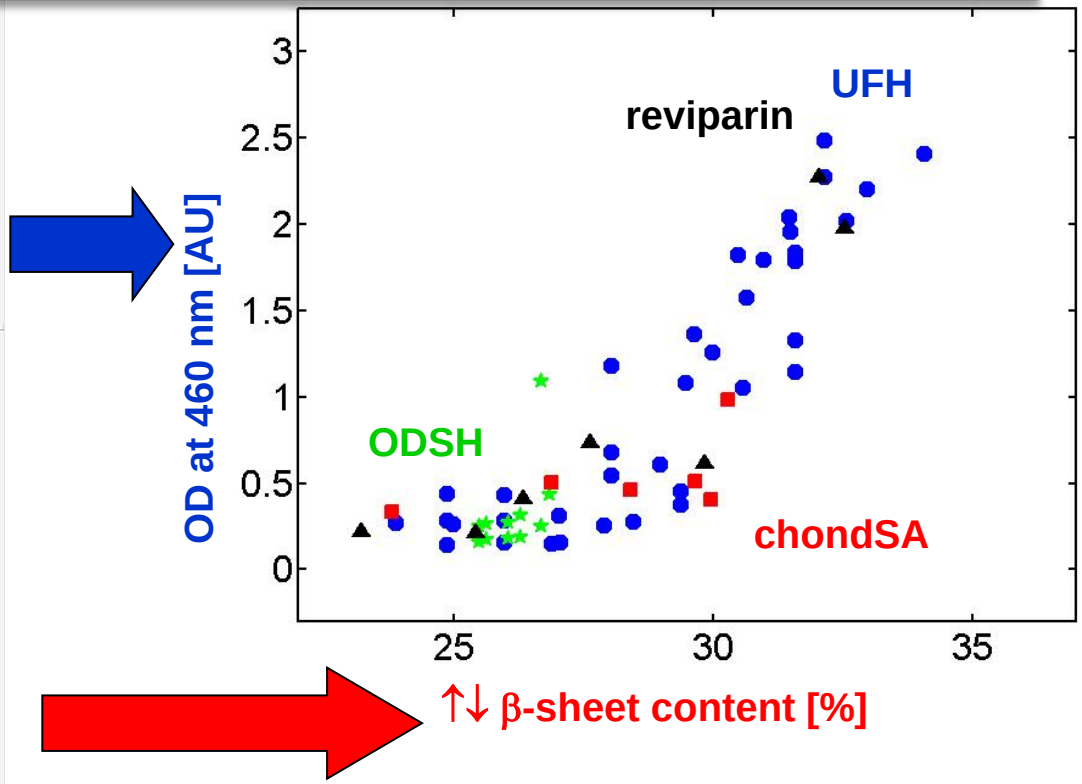




- 1x PBS, NaCl [150 mM], 25 ° C
- PF4 [1.25*10^{-6} M]

Brandt S. et al., T&H 2014

First example for predictive testing of new drugs for immunogenicity risk



Brandt S. et al., T&H 2014

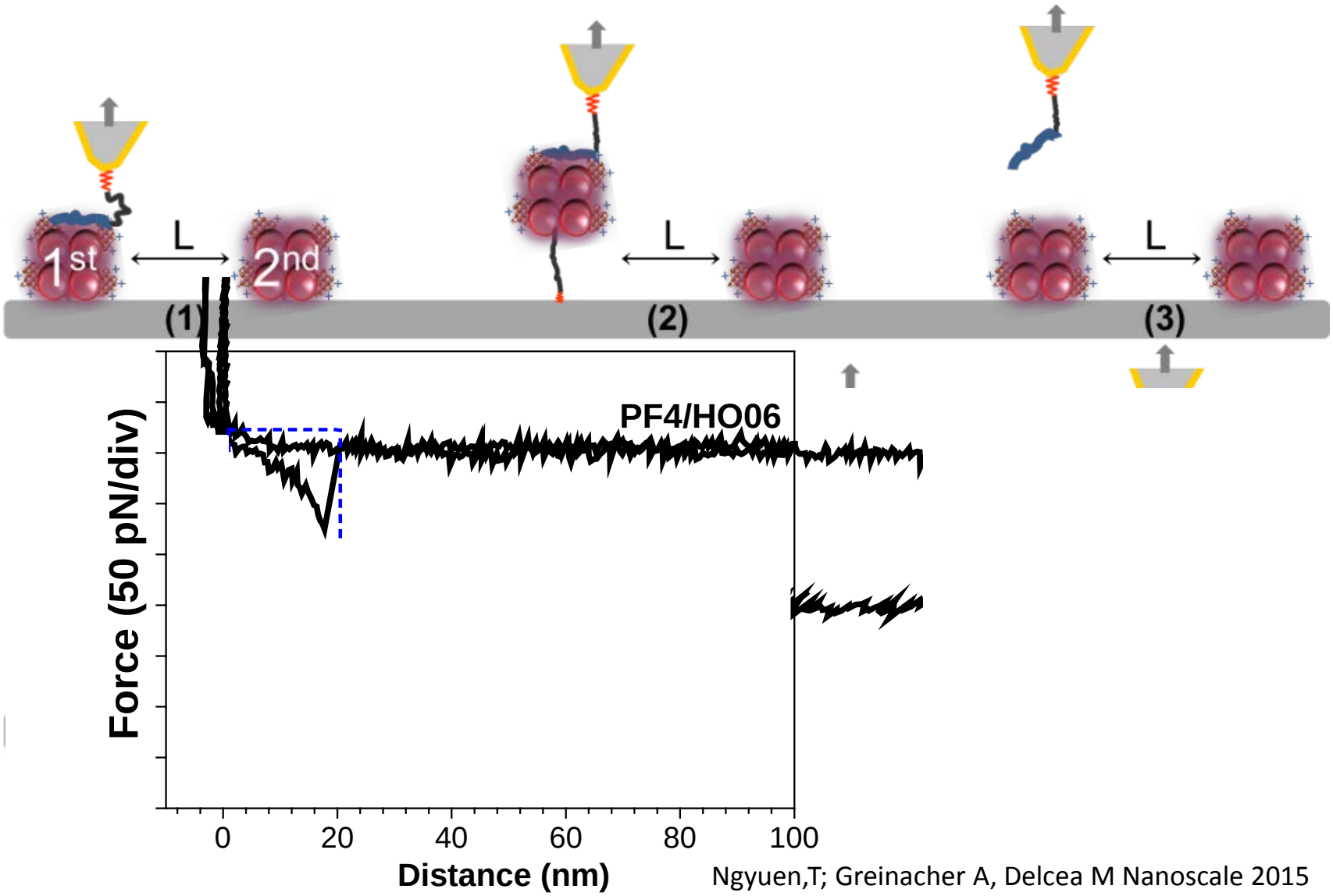
HO16 and UFH provide enough energy for the structural change of PF4

Complexes	Enthalpy, ΔH [kcal/mol]		ΔH structural change in PF4 [kcal/mol]
PF4/UFH	-6682±1150	>	~4200
PF4/HO16	-7260±1365	>	
PF4/HO08	-4240±1467	≈	
PF4/HO06	-2071±35	<	
PF4/fondaparinux	-1333±57	<	

Kreimann M., et al. BLOOD 2014

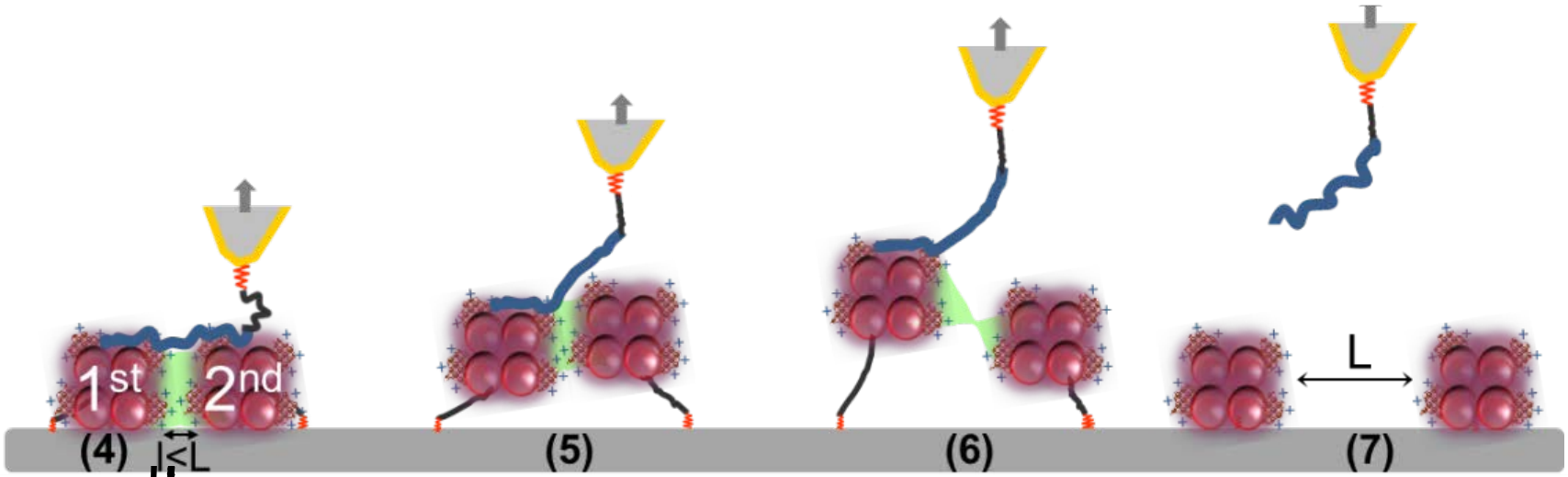
Why do polyanions which neutralize the charge induce different energy profiles?

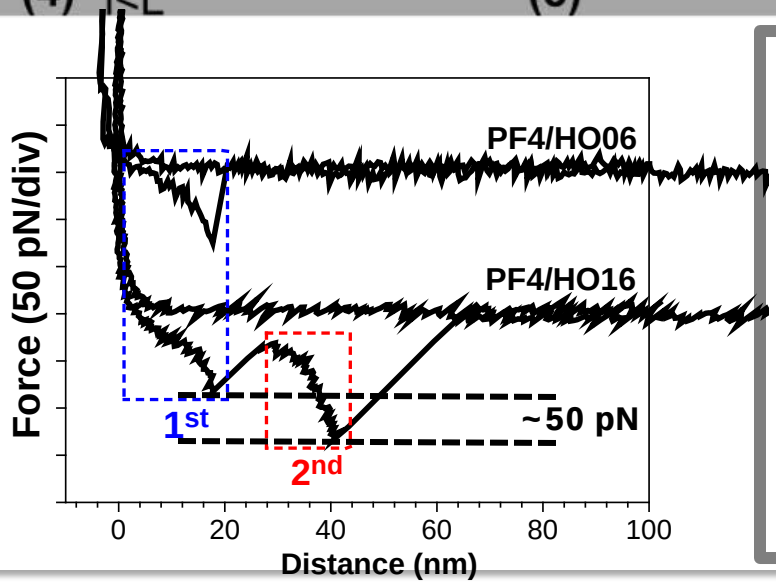
PF4/Heparin Binding in SMFS Experiment

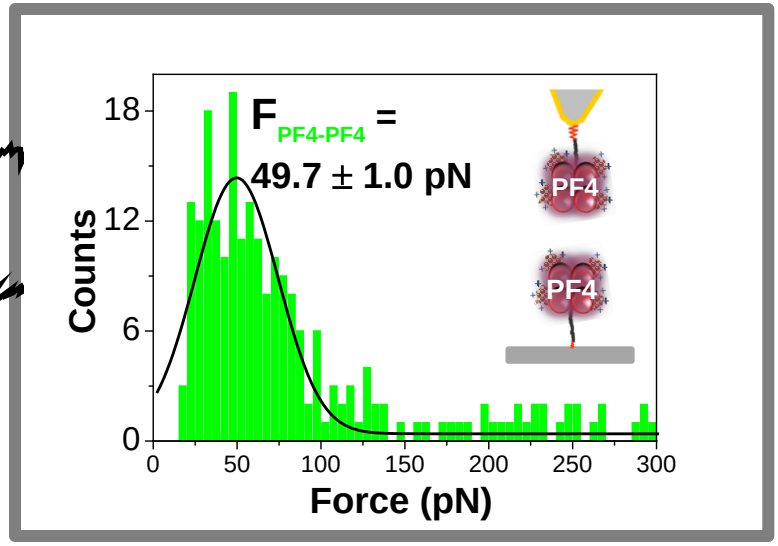


Ngyuen,T; Greinacher A, Delcea M Nanoscale 2015

PF4/Heparin Binding in SMFS Experiment







Ngyuen,T; Greinacher A, Delcea M Nanoscale 2015

Fragestellungen

- Thrombozyten – Bakterien-Interaktionen
- Thrombozyten – Viren Interaktionen

- Polyanionen als Trigger der Immunabwehr
- Übergang in Autoimmunreaktionen