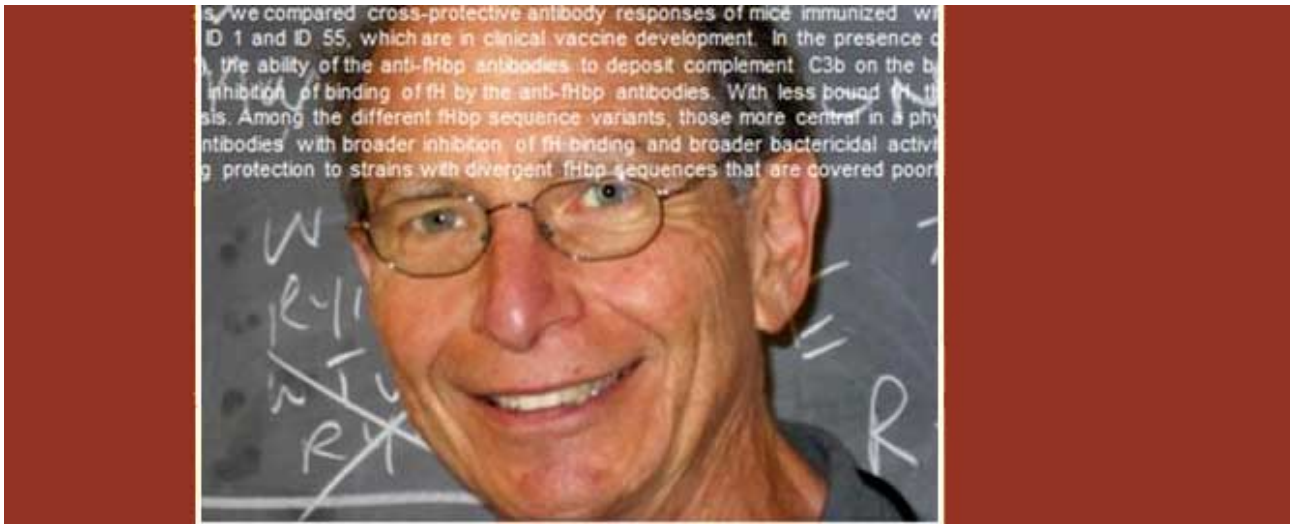
NOVARTIS

Seminari



Speaker

Dan M. Granoff, M.D.

Clorox Endowed Chair and Director, Center for Immunobiology and Vaccine Development, Children's Hospital Oakland Research Institute, California USA

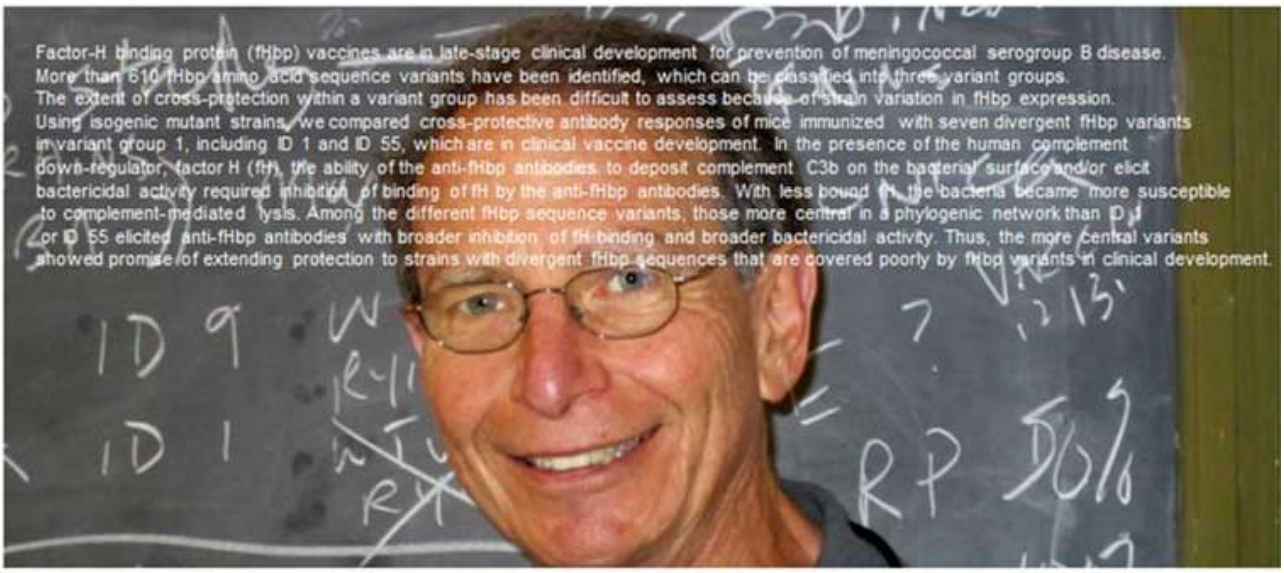
Host

M. Pizza

Presents

Importance of inhibition of binding of complement factor H for serum bactericidial antibody responses to meningococcal factor H-binding protein vaccines

11 dicembre 2012, ore 12.00
Auditorium Research Center
Via Fiorentina, 1 - Siena


Factor-H binding protein (fHbp) vaccines are in late-stage clinical development for prevention of meningococcal serogroup B disease.
More than 610 fHbp amino acid sequence variants have been identified, which can be classified into three variant groups.
The extent of cross-protection within a variant group has been difficult to assess because of strain variation in fHbp expression.
Using isogenic mutant strains, we compared cross-protective antibody responses of mice immunized with seven divergent fHbp variants
in variant group 1, including ID 1 and ID 55, which are in clinical vaccine development. In the presence of the human complement
down-regulator, factor H (fH), the ability of the anti-fHbp antibodies to deposit complement C3b on the bacterial surface and/or elicit
bactericidal activity required inhibition of binding of fH by the anti-fHbp antibodies. With less bound fH, the bacteria became more susceptible
to complement-mediated lysis. Among the different fHbp sequence variants, those more central in a phylogenic network than ID 1
or ID 55 elicited anti-fHbp antibodies with broader inhibition of fH binding and broader bactericidal activity. Thus, the more central variants
showed promise of extending protection to strains with divergent fHbp sequences that are covered poorly by fHbp variants in clinical development.