Herpesviruses: Pathogenesis and Cancer

(How HSV interferes with the normal functions of its cellular receptors)

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Current:
Gabriel Haila (Biochemistry)
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Graduated:
Kevin DAmico (CHOP) ‘16
Paul Rothlauf (Harvard) ‘17
Abe Hakim (Cooper Medical School at RU) ‘17
Rebecca Murray (teaching) ‘17

Ongoing lab projects:
Effects of HSV on the functions of its receptors (cellular, immunological).
Characterization of antiviral compounds.
Isolation of bacteriophages from honeybee microflora.

Rowan collaborators:
Chun Wu (Chemistry)
Subash Jonnalagadda (Chemistry)
Lana Vojvodic (Biology)

Rowan funding:
Rowan University SEED funding
College of Science and math start-up funds

External collaborators:
Gary Cohen and Roz Eisenberg (PENN)
Xiao Zhang and Bing-chun Zhao (Sun Yat-sen Univ., Guangzhou)
Jose-Antonio Lopez-Guerrero (Univ. of Madrid)
Professor of Microbiology
Laboratory Head, Laboratory of Microbiology
Department of Pathobiology School of Veterinary Medicine

Fellow, American Academy of Microbiology.
Fellow, American Association for the Advancement of Science.

Lenore Rowe Williams Award, UPENN, 2006, for outstanding scientific contributions and leadership as well as mentorship of the next generation of aspiring women scientists.

194 peer reviewed articles
18 reviews or book chapters
(Cited 12415 times in 5119 articles)
>> 200 abstracts, posters
8 patents
Several NIH grants
Eisenberg RJ et al. 188 published article abstracts 1973-2017
How to understand HSV entry glycoproteins.

What does it do?
What does it look like?

Attachment

Receptor binding

Conformational changes

Membrane fusion

HSPG

Nectin-1

HVEM

gC

gB

gHgL

1

2

3

4

5

fusio
What does it do?
What does it look like?

Purify proteins.
- Recombinant baculoviruses
  (grams of highly purified proteins since 1994)

Generate antibodies.
- Polyclonals (274 rabbit sera)
  and monoclonals (TMTC)

Embrace new technologies.
- Biosensors
- Live cell fluorescence microscopy
- Bimolecular fluorescence complementation
- Molecular biology (> 1112 plasmids)
- Molecular modeling

Collaborate.
Crystallography
  Don Wiley (Harvard)
  Stephen Harrison (Harvard)
  Andrea Carfi (Merck/ Novartis)
  Katya Heldwein (Tufts)

Receptors
  Pat Spear (Northwestern U)

Vaccines
  Harvey Friedman (PENN)
  Small and large companies
  And others…

How to understand HSV entry glycoproteins.
Nectin-1 binding to gD

Displacement of the gD C-terminus

Exposure of gD C-terminus

Activation of prefusion gB

Activation of gHgL

Extension and fold-back of gB

Fusion

*N Hypothetical structure of C-terminus

HSV entry glycoproteins: what they do and what they look like!
CIRCA 1982

CIRCA 1985: Epitope mapping and molecular modeling (collab. E. Golub)

CIRCA 1990: introduction of Art. Initial folding
1992: map of disulfide bonds. Roles of carbohydrates

1994: Baculovirus production (gD306t)
1994: Identification of 4 functional regions (FR)
1994-2000: Bac production of gD variants to analyze functional regions

1995: more folding
Structure-function analysis
2001: crystal structure of gD (collab: D. Wiley and A. Carfi).
Arrangement of FR confirmed
Disulfide bonds confirmed

1994: Baculovirus production (gD306t)
1994: Identification of 4 functional regions (FR)
1994-2000: Bac production of gD variants to analyze functional regions
These structures are at the basis of the current functional model of activation of gD by its two main, and very different, receptors.
The contribution of Roz, and Gary, has been and will continue to be absolutely fundamental in the field of virology, beyond HSV entry.

Roz influenced many labs by mentoring new scientists and sharing a philosophy of science, an approach to studying viral glycoprotein functions and many reagents with many labs. (try to find a paper on herpesvirus entry that does not acknowledge this contribution!)
Thank you Roz, Happy retirement!