Death in 5 Genes
Suggested Model of Rabies Key Protein

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Background

- Rabies is a viral disease that affects warm blooded animals, and can be transmitted from one species to another.
- The rabies virus travels to the brain by following the peripheral nerves, and causes acute encephalitis.
- The disease is fatal for humans, and once symptoms have presented, survival is rare, even with the administration of proper and intensive care.
- The Rabies virus, part of the Rhabdoviridae family, has a single strand anti sense RNA.
- The virus genome is encoded to only 5 genes, one of which is P. The P gene is encoded to Phosphoprotein (P protein), and 4 other short products of P: p2:p5.
- P protein is a cofactor of L polymerase, and also known to have a roll in decreasing the immune response of the host.

Material and methods

- Gene Bank – Sequence Database, used to find the sequence of P protein.
- PDB - Retrieve both STAT and P protein tertiary structures.
- JASPAR - find transcription factor-STAT1 binding sites on the DNA.
- PFP - locate the longest positive/negative patch. Used to find the DNA binding domain in STAT1/P, or the STAT1 binding domain in P.
- PfAM - used to find protein-protein binding domain on P protein.
- Intervor – used to find amino acid residues that have high probability of binding to the DNA.

Results

- Previous researches show that Rabies virus P protein inhibits TF-STAT1 function in at least two different ways:
  - By retaining phosphorylated STAT1 in the cytoplasm.
  - By inhibiting STAT1 binding to the DNA.
- For the first inhibition form to be made possible, we figured there has to be a protein-protein binding domain on both proteins. Therefore, we searched for known domains on both proteins - STAT1 and P Protein. A single SH2 domain was found on STAT1, whereas no known domains were found on P.

Conclusions

- P protein contain a large positive patch, that might serve as DNA binding domain to STAT motif, that inhibits STATs function. Nevertheless, the positive patches of STAT1 and P protein do not have a similar tertiary structure.
- P protein contains a large negative patch, that might serve as protein-protein binding domain, that binds DNA binding domain of STAT1 and thus inhibits STAT1 ability to contact the DNA.
- P protein assists the virus to cope with the host immune system.

Goals

- Find a Rabies protein that affects the host transcription, and try to suggest a model for its way of function.
- Show the effect of the viral protein on the host.

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References