



Topics in Viral Immunology
Bruce Campell
Supervisory Patent Examiner
Art Unit 1648



IS THIS METHOD OBVIOUS?

- **Claim:** A method of vaccinating against CPV-1 by...
- **Prior art:** A method of vaccinating against CPV-2 by [same method as claimed].



HOW ARE VIRUSES CLASSIFIED?

Source:

Seventh Report of the International Committee on Taxonomy of Viruses (2000)

Edited By M.H.V. van Regenmortel, C.M. Fauquet, D.H.L. Bishop, E.B. Carstens, M.K. Estes, S.M. Lemon, J. Maniloff, M.A. Mayo, D. J. McGeoch, C.R. Pringle, R.B. Wickner

***Virology Division
International Union of Microbiological Sciences***



TAXONOMY - HOW ARE VIRUSES CLASSIFIED?

- **Example: Potyvirus family (Potyviridae)**
- **Example: Herpesvirus family (Herpesviridae)**



Potyvirus

- **Plant viruses**
- **Filamentous particles, 650-900 nm**
- **+ sense, linear ssRNA genome**
- **Genome expressed as polyprotein**



Potyvirus Taxonomy - Traditional

- **Host range**
- **Transmission (fungi, aphids, mites, etc.)**
- **Symptoms**
- **Particle morphology**
- **Serology (antibody cross reactivity)**



Potyviridae Genera

- **Bymovirus** – bipartite genome, fungi
- **Rymovirus** – monopartite genome, mites
- **Tritimovirus** – monopartite genome, mites, wheat
- **Potyvirus** – monopartite genome, aphids
- **Ipomovirus** – monopartite genome, whiteflies
- **Macluravirus** – monopartite genome, aphids, bulbs

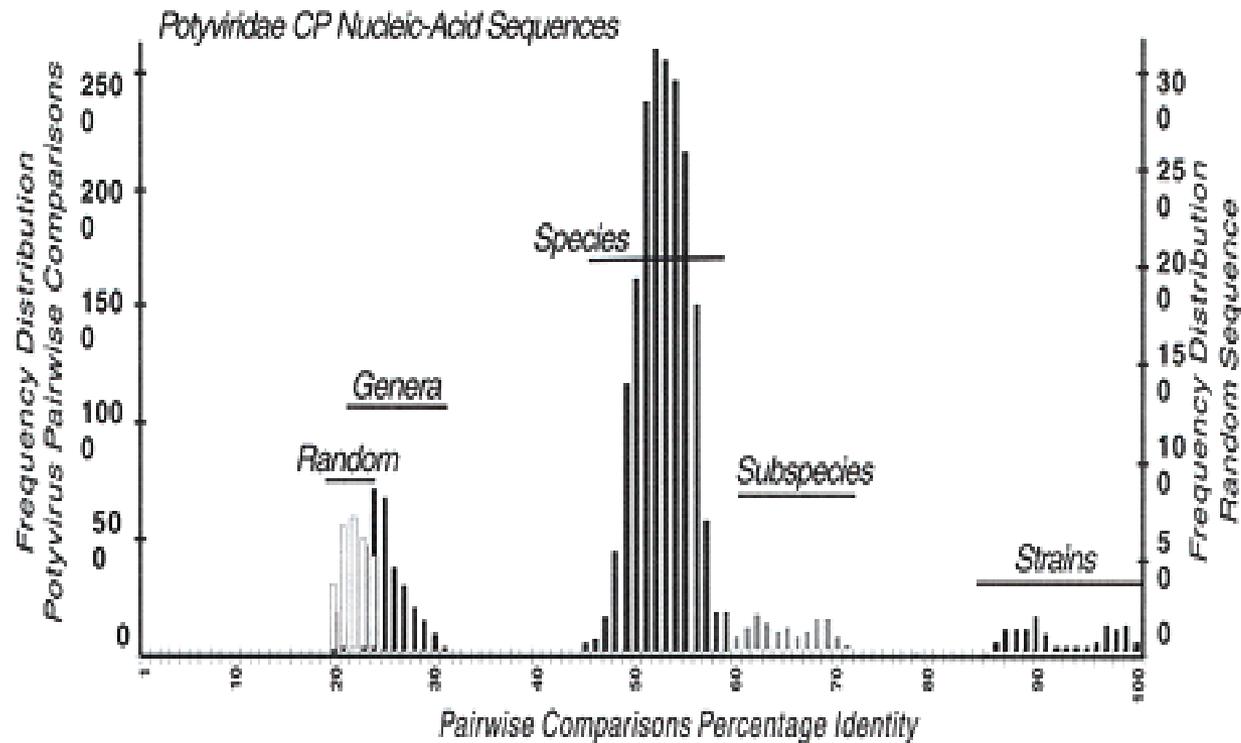


Potyvirus Taxonomy - Molecular

- **Polyprotein cleavage sites**
- **% similarity of coat protein sequences**
- **Genomic sequences – many complete genomic sequences, >200 coat protein sequences now available for comparison**



Coat Protein Sequence Comparison (RNA)





Potyviridae Species

- **Bymovirus – 6 species**
- **Rymovirus – 4-5 species**
- **Tritimovirus – 2 species**
- **Potyvirus – 85 – 173 species**
- **Ipomovirus – 1-2 species**
- **Macluravirus – 2 species**



Higher Order Virus Taxonomy

- **Nature of genome: RNA or DNA; ds or ss (+/-); linear, circular (supercoiled?) or segmented (number of segments?)**
- **Genome size – 11-383 kb**
- **Presence of envelope**
- **Morphology: spherical, filamentous, isometric, rod, bacilliform, etc.**
- **Host range**



HOW ARE VIRUSES CLASSIFIED?

- **Example: Potyvirus family (Potyviridae)**
- **Example: Herpesvirus family (Herpesviridae)**

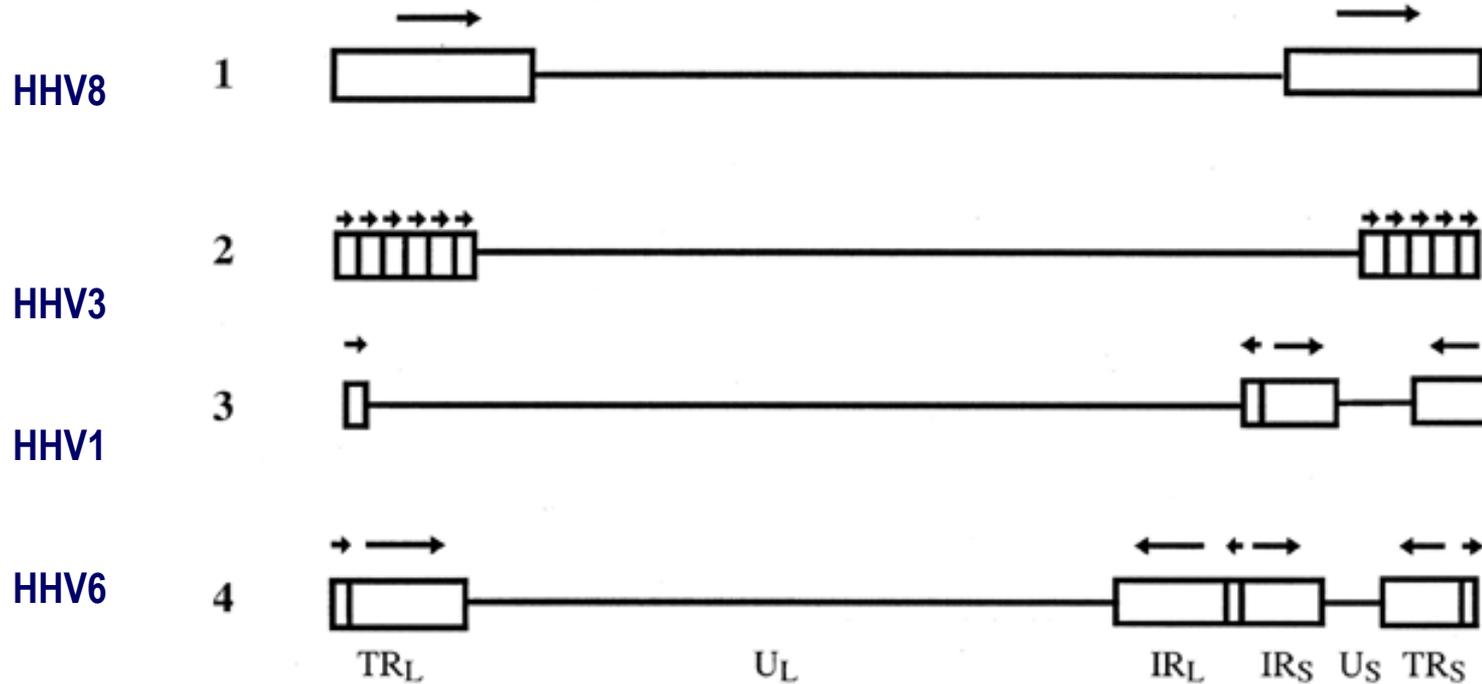


Family Herpesviridae

- dsDNA, one linear segment, 125 – 240 kbp
- Enveloped
- Isometric
- Infect vertebrates



Herpes Genome Organization



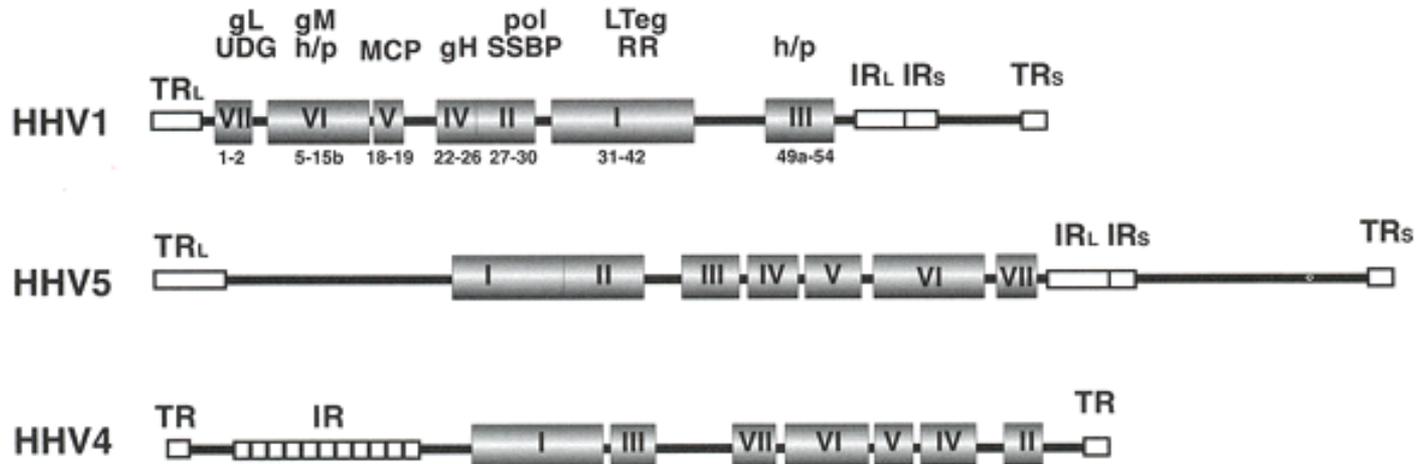


Herpes Genome Organization

- **70 – 200 ORFs**
- **In avian and mammalian viruses, about 40 conserved genes arranged in 7 blocks**
- **Viruses infecting fish and amphibians have less sequence conservation (classification based more on morphology)**



Herpes Genome Organization





Family Herpesviridae

- **Subfamily Alphaherpesvirinae**
- **Subfamily Betaherpesvirinae**
- **Subfamily Gammaherpesvirinae**
- **Unassigned genus Ictalurid Herpes-like Viruses**



Subfamily Alphaherpesvirinae

- **Molecular analysis shows it to be a distinct lineage within the family**
- **U_s , IR_s and TR_s homologous to HHV 1**
- **Many members cause overt epithelial lesions in their hosts**



Subfamily Alphaherpesvirinae

- Genus Simplexvirus: 9 species; HSV-1, HSV-2
- Genus Varicellovirus: 16-18 species; VZV
- Genus “Marek’s Disease-like Viruses”: 3 species; MDV
- Genus “Infectious Laryngotracheitis-like Viruses”: 1 species
- Unassigned species: 3



Subfamily Betaherpesvirinae

- **Molecular analysis shows it to be a distinct lineage within the family**
- **Genes corresponding to U_s 22 family of HHV 5 are characteristic of the subfamily**
- **Often species-specific and cell-type specific, with no clinical symptoms**



Subfamily Betaherpesvirinae

- Genus Cytomegalovirus: 3-5 species; hCMV
- Genus Muromegalovirus: 2 species; muCMV
- Genus Roseolovirus: 2-3 species; HHV 6
- Unassigned species: 1



Subfamily Gammaherpesvirinae

- **Molecular analysis shows it to be a distinct lineage within the family**
- **Genes corresponding to BNRF, BTRF and BRLF of HHV 5 are characteristic of the subfamily**
- **Many members infect lymphocytes and are associated with malignancies and other lymphoproliferative disorders**



Subfamily Gammaherpesvirinae

- Genus Lymphocryptovirus: 7 species; EBV
- Genus Rhadinovirus: 13-18 species; HHV 8 (KS associated)



Family Herpesviridae

- **Unassigned genus “Ictalurid Herpes-like Viruses”:** 1 species, channel catfish virus
- **Unassigned species:** 47; infect mammals, fish, birds, reptiles, molluscs



Implications for Patentability

Enablement / Obviousness:

- **Scope of the claims – size of virus taxon?**
- **Predictability of the art – how similar are family members, how well are they characterized?**



Implications for Patentability

Written Description for New Species

- Is genomic sequence necessary?
- Is genomic sequence sufficient?
- Other factors to consider: particle size and morphology, genome size and type, host species, symptoms, serological data



Implications for Patentability

Written Description for New Species

Is genomic sequence necessary?

USP 7,351,527

1. An isolated avirulent form of a CV DNA virus that causes viral disease in fish, the CV DNA virus being a double stranded DNA virus having a capsid with a icosahedron morphology, the capsid being of about 90-110 nm in size as determined by electron microscopy, the DNA of the CV DNA virus having between about 250,000 and 300,000 base pairs.



Implications for Patentability

Written Description for New Species

Is genomic sequence sufficient?

1. **An antibody or antiserum directed against a virus comprising in a non-coding region of the viral genome an RNA sequence corresponding to a cDNA sequence shown in Seq ID No:1 or a cDNA sequence having at least 75% sequence identity to Seq ID No:1, whereby said virus causes mammalian disease.**



Implications for Patentability

- **Definiteness**

Claim 1. An HIV NEF protein having a glutamine residue at position 53.



HIV NEF SEQUENCE ALIGNMENT

WO 2006/018289

PCT/EP2005/008907

4/8

```
NEF_HIV1U4      MGGKWSKKS RVEWPEVRKRMRETP---AAK-----GVGAVSQ-----DLDKYG-
NEF_HIV1EL      MGGKWSKSSIVGWPAIRERIRRTN---PAAD-----GVGAVSR-----DLEKHG-
NEF_HIV1ZH      MGNKWSK----GWPAVRERIRQTTPAPPAAE-----GVGAAASQ-----DLAKHG-
NEF_HIV112      MGGKWSKSSVVGWPAVRERMRAE---PAAD-----GVGAAASR-----DLEKHG-
NEF_HIV1B1      MGGKWSKSSVVGWPTVRERMRAE---PAAD-----GVGAAASR-----DLEKHG-
NEF_HIV1SC      MGGKWSKRSVVGWPTVRERM RKTE---PAAD-----GVGAAASR-----DLEKHG-
NEF_HIV1JR      MGGKWSKHSVPGWSTVRERMRAE---PATDRV RQT E PAAVGVGAVSR-----DLEKHG-
NEF_HIV1MA      MGGKWSKSSIVGWPKIRERIRRTN---PTET-----GVGAVSQDAVSQDLDKCG-
NEF_SIVCZ       MGTKWSKSSLVGVPEVRRRIREAP---TAAE-----GVGEVSK-----DLERHG-
NEF_SIVS4       MGGAI SKKQYKRGNLRERLLQARGETYGR LWEGLEEGYSQSLGASGKGLSSLSCEPQKY
NEF_SIVM1       MGGAI SKKRSKPPRDLRQRLLRARGENYGR LFKGVEDGSSQSLGGLDKGLSSLSCEGQKY
NEF_HIV2SB      MGASGSKKRSRPSRGLQERLLRARGGACGGLWDESEGGYSQFHEGSGREQKLPSC EGQRY
NEF_HIV2RO      MGASGSKKHSRPPRGLQERLLRARAGACGGYWNESGGEYSRFQEGSDREQKSPSCEGRQY
NEF_HIV2ST      MGASGSKKRSEPSRGLRERLLQTPGEASGGHWDKLGGEYLSQEGSGRGQKSPSCEGRRY
NEF_HIV2CA      MGASGSKKRSRPLQGLQERLLRARAGTCGECYNAL EGESLRSQEGSDREQNSLSC EGQRY
NEF_HIV2BE      MGASGSKKLSKHSRGLRERLLRARGDGYGKQRDASGGEYSQFQEGSGREQNSPSC EGQRY
NEF_HIV2D2      MGSAGSKKRSE RQQGLREKLLRVPERPYGR LSGERREQSSRSPGESDKDLNSPSC EGQ--
NEF_SIVAI       MGSNSKRQQQLLKLWRGLRGKPGADWVLLSDPLIGQSSTVQE ECGKALKKSWGK----
NEF_SIVA1       MGLGSSKPQHKKQLTIWRALHATR HTRYGLLADPLIGQSSTLQE ECDKGLRKS LIRKRN-
NEF_SIVGB      MGSQSKKRSEAWVRYSSALRQLVGG-----PVT PDGYKQIESSQGA EKQSLLRGRAY
```

** ** :



Implications for Patentability

■ Definiteness

Claim 1. An HIV NEF protein having a glutamine residue at position 53.

Better:

Claim 2. An HIV NEF protein having a glutamine residue at the position corresponding to position 53 of SEQ ID NO: 1.

Note that the NEF protein is very well known in the art.



Implications for Patentability

- **Every case presents a unique fact situation.**
- **No *per se* rules.**



Thanks for listening!

Bruce Campell

Supervisory Patent Examiner

Art Unit 1648

Bruce.Campell@uspto.gov

571-272-0974