Newcastle disease virus

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Newcastle disease

- First identified in Newcastle in 1926
- Affects all species of birds
- Mortality up to 100% in chickens
- Widespread in Asia, Africa, Europe and South America
- In USA, sporadic Newcastle disease (ND) occur due to importation of infected birds.
- In 2002 ND outbreak in California, four million birds were depopulated and cost the U.S. billions of dollars in damage and lost trade.
- NDV is a threat to the U.S. poultry industry and is listed as a select agent.

Newcastle disease virus

- A member of the genus *Avulavirus* in the family *Paramyxoviridae*
- The genome is a single-stranded negative-sense RNA consisting of 15,186 nucleotides
- The genome contains six genes in the order of 3'-NP-P-M-F-HN-L-5'
- The virus is enveloped, roughly spherical, with a diameter around 100-500nm.
- F and HN proteins form the external envelope spikes
- V and W proteins are produced from the P gene by alternative mRNAs that are generated by RNA editing.

NDV natural isolates

- Based on severity of disease, NDV isolates are grouped into three pathotypes:
  - Lentogenic strains
    - Cause mild or inapparent respiratory disease
  - Mesogenic strains
    - Cause respiratory or nervous signs with moderate mortality
  - Velogenic strains
    - Cause severe intestinal and/or neurologic disease resulting in high mortality
      - Neurotropic
      - Viscerotropic

Examples of pathogenicity indices obtained for strains of Newcastle disease virus.

Virus Strain	Pathotype	ICPI[a]	IVPI[b]	MDT[c]
Ulster 2C	Lentogenic	0.0	0.0	>150
Queensland V4	Lentogenic	0.0	0.0	>150
Hitchner B1	Lentogenic	0.2	0.0	120
F	Lentogenic	0.25	0.0	119
LaSota	Lentogenic	0.4	0.0	103
H	Mesogenic	1.2	0.0	48
Mukteswar	Mesogenic	1.4	0.0	46
Roakin	Mesogenic	1.45	0.0	68
Beaudette C	Mesogenic	1.6	1.45	62
GB Texas	Velogenic	1.75	2.7	53
NY Parrot 70181 1972	Velogenic	1.8	2.6	51
Italien	Velogenic	1.85	2.8	50
Milano	Velogenic	1.9	2.8	50
Herts '33/56	Velogenic	2.0	2.7	48

[a]ICPI, intracerebral pathogenicity index in day-old chicks
[b]IVPI, intravenous pathogenicity index in 6-week-old chickens
[c]MDT, mean death time (hr) for chicken embryos infected with one minimum lethal dose of virus
(Adapted from *Diseases of Poultry*)

Relationship to human pathogens

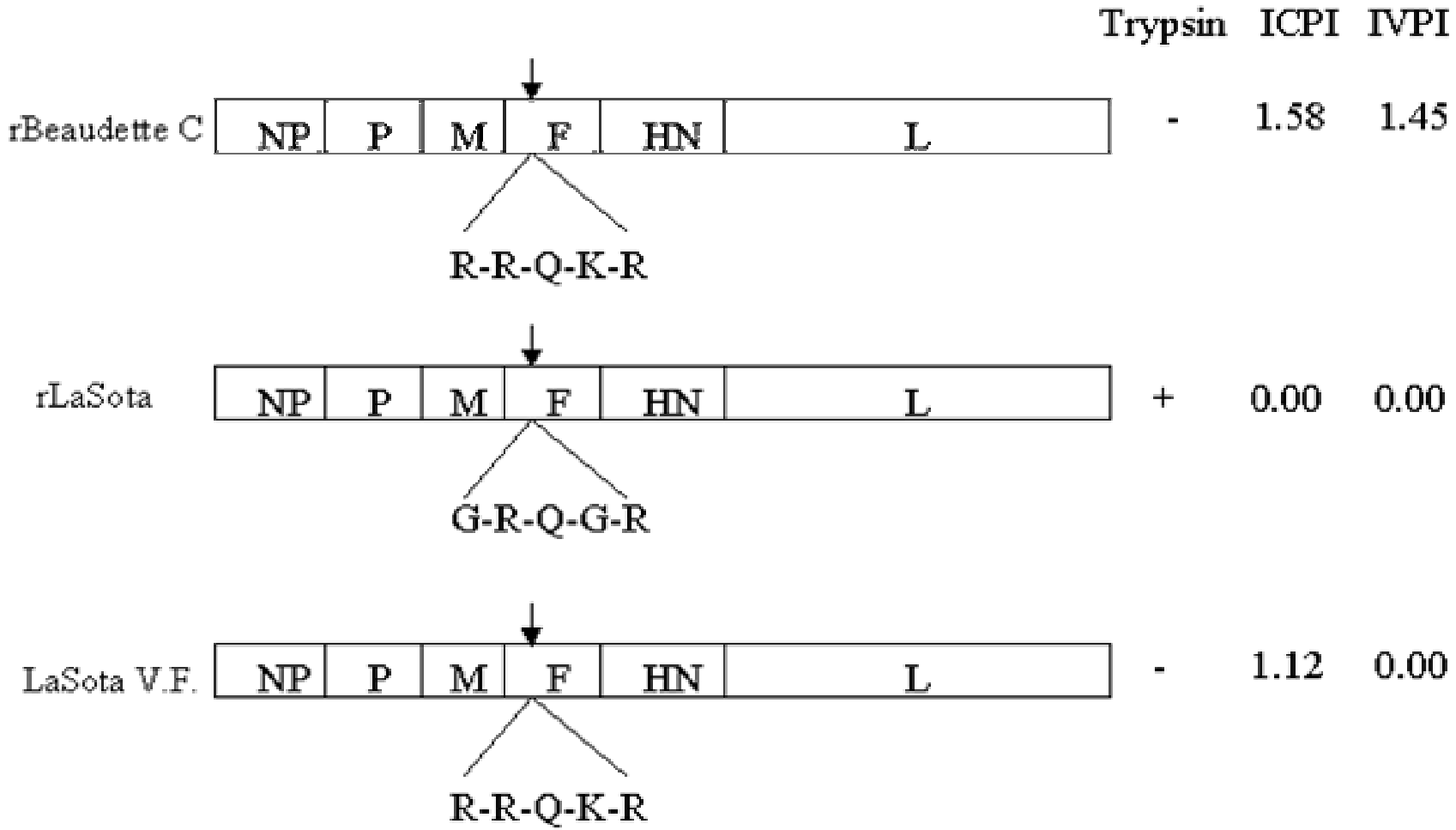
- Closely related to human paramyxoviruses such as measles, mumps, human parainfluenza and respiratory syncytial virus, and the emerging pathogens, Nipah and Hendra viruses.

- Distantly related to lethal filoviruses, Ebola and Marburg, and the rhabdovirus, rabies.

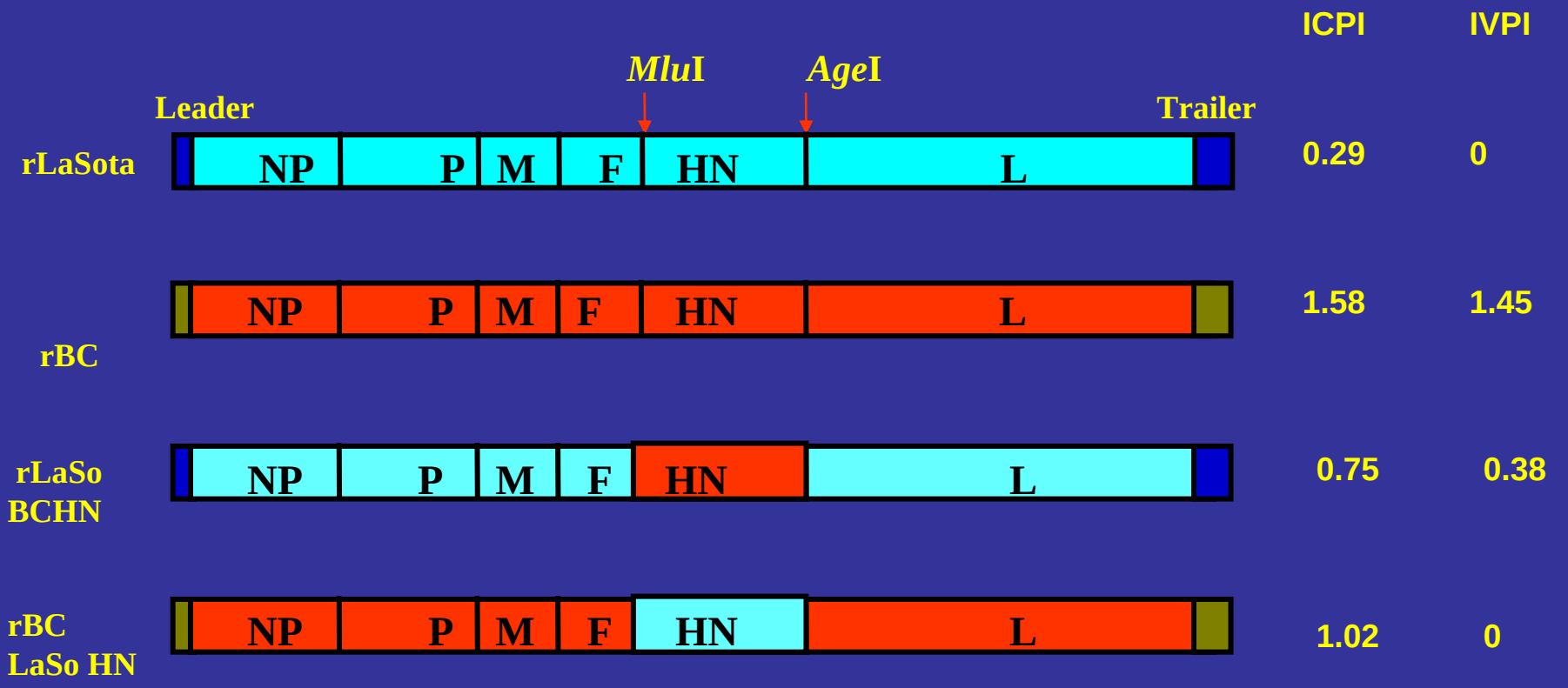
NDV studies using reverse genetics

- Molecular Pathogenesis
  - Role of F, HN and V proteins in virulence
  - Glycosylation of HN and virulence
- Vaccine development
  - Improved Vaccines
  - Vaccine Vectors

Fusion Protein and Virulence

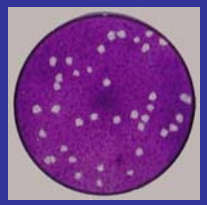


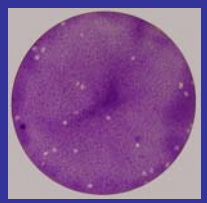
HN Protein and Virulence

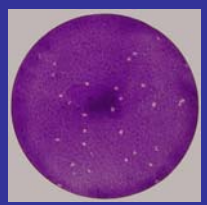


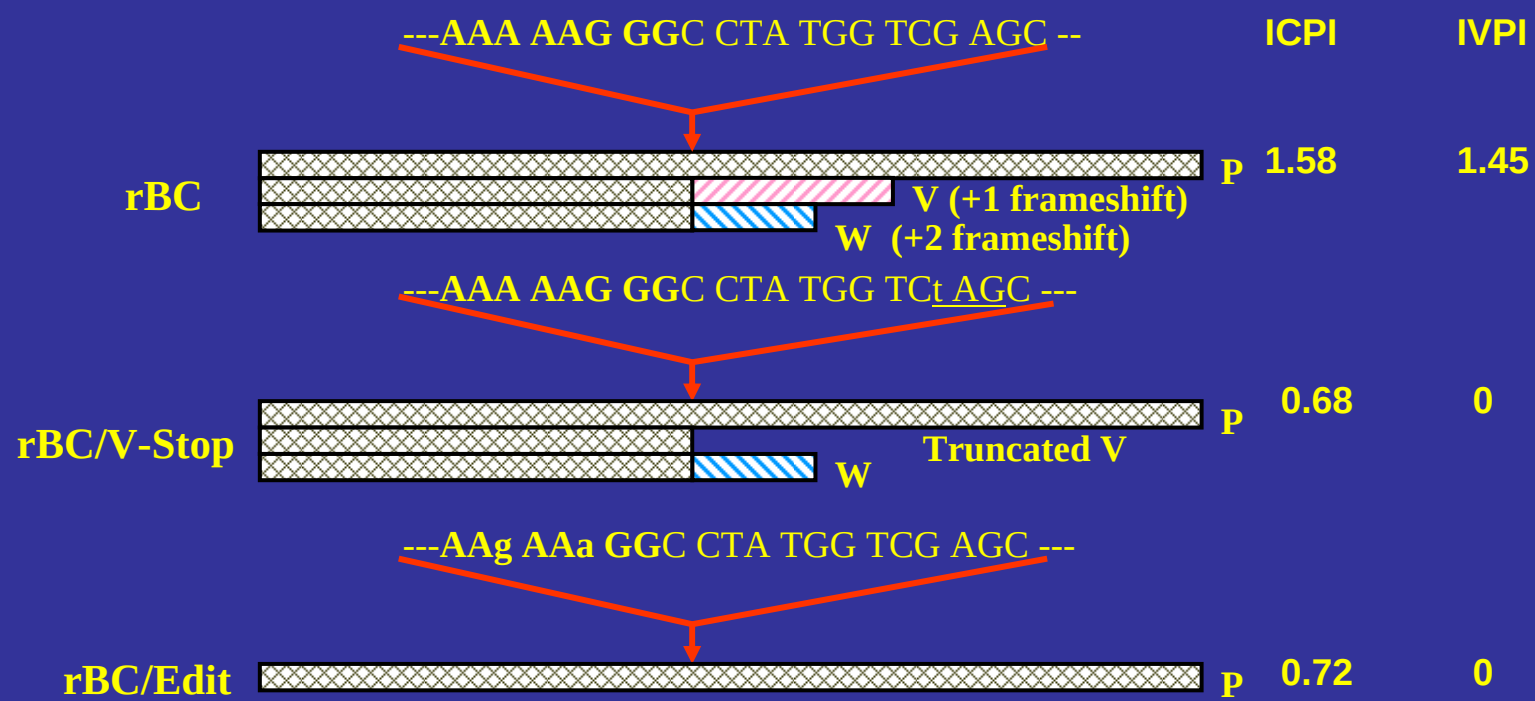
V Protein and Virulence

RNA editing -P gene

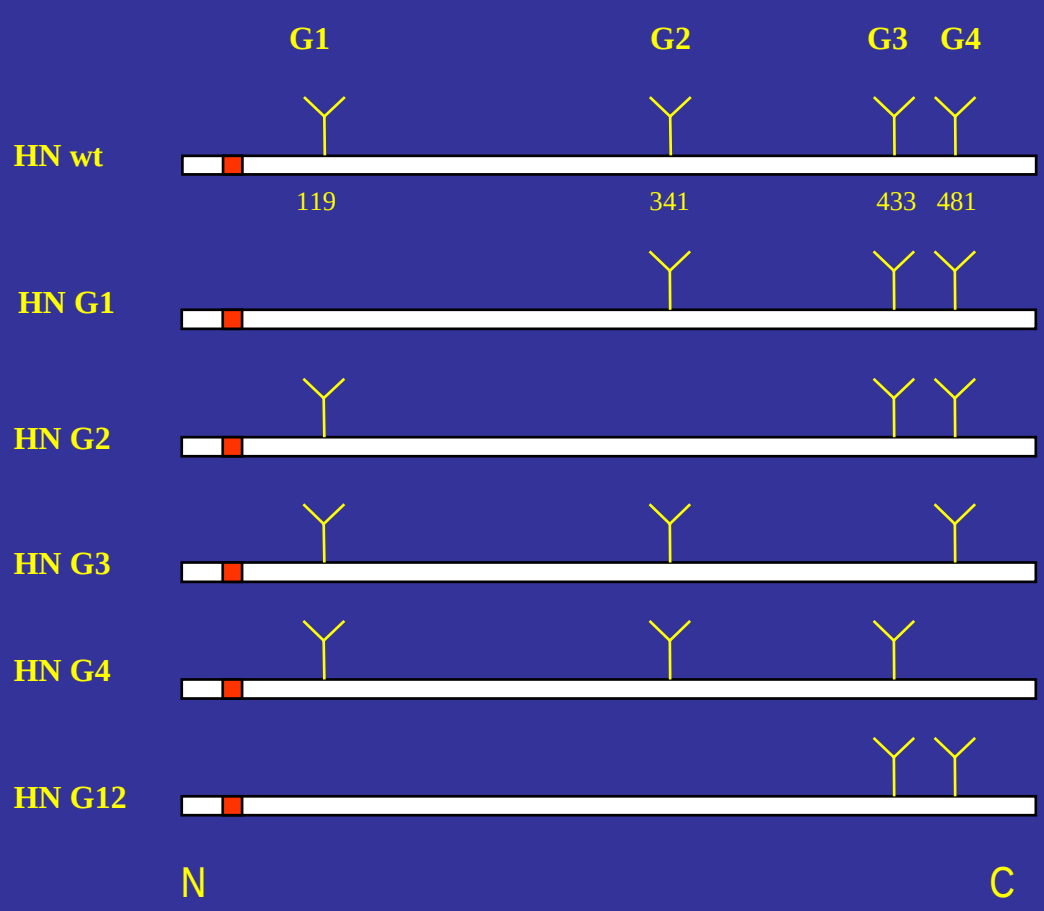






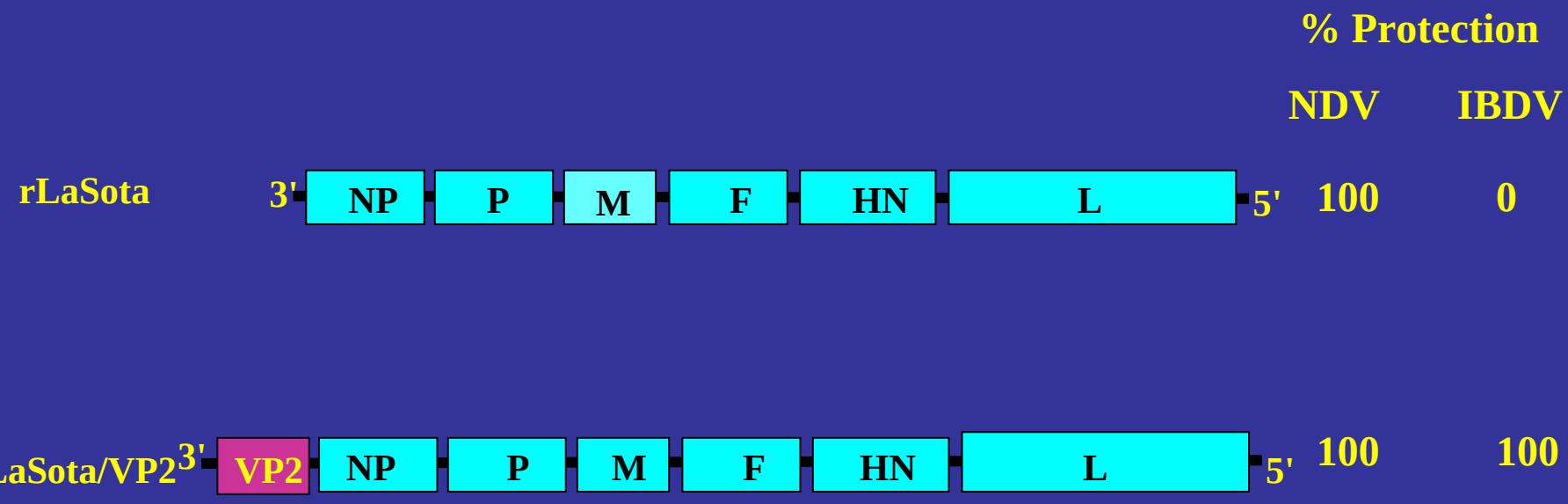


HN protein glycosylation and Virulence



	ICPI	IVPI
HN wt	1.50	1.32
HN G1	1.12	0.37
HN G2	0.87	0.44
HN G3	1.07	0.75
HN G4	0.66	0.31
HN G12	0.76	0.67

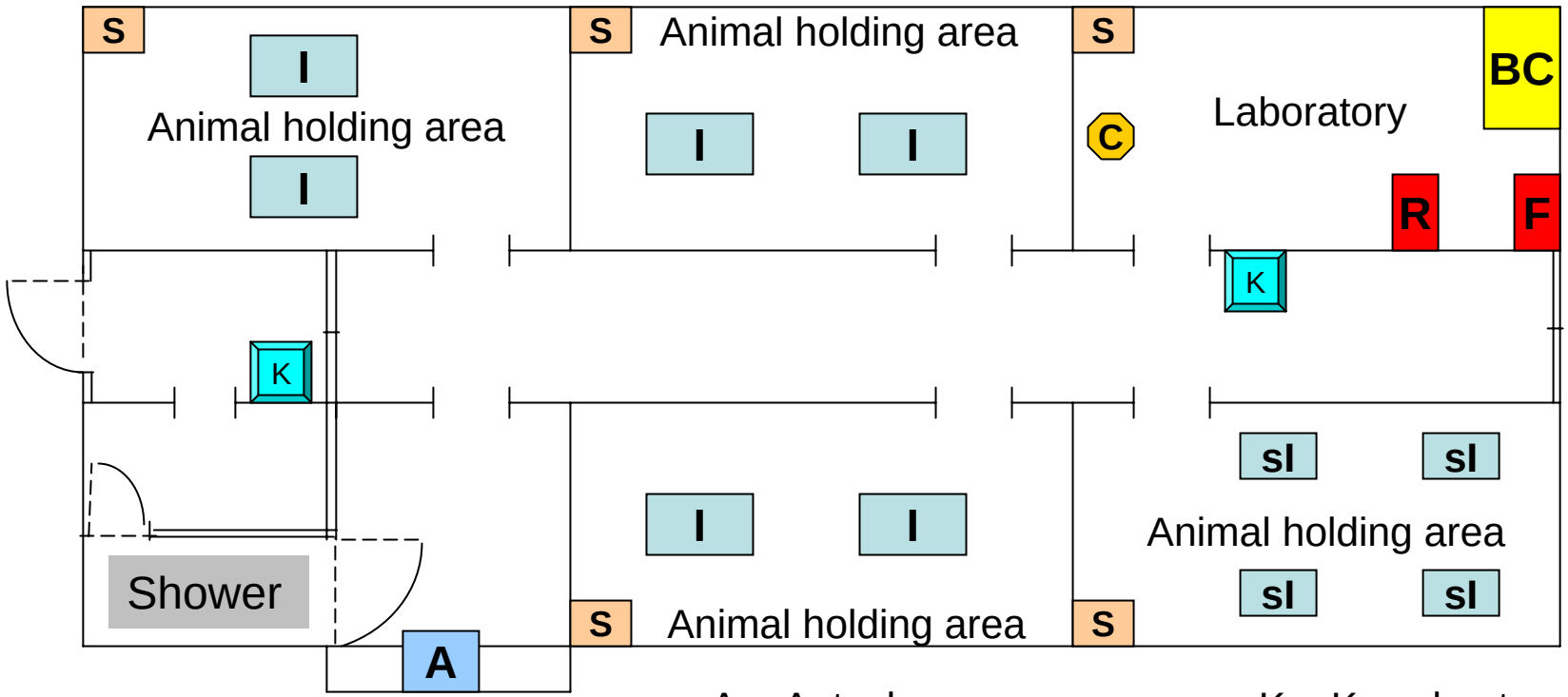
Newcastle Disease Virus as a Vaccine Vector for Infectious Bursal Disease Virus (IBDV)



Current studies

- Role of individual NDV proteins in pathogenesis
- NDV-vectored human vaccines
- NDV-vectored veterinary vaccines
- NDV as an oncolytic agent

Floor Plan of Bio-Safety Level 3 Facility at University of Maryland



A – Autoclave
BC – Bio Safety Cabinet
C – Centrifuge
F – Freezer
I – Isolator

K – Key chest
R – Refrigerator
S – Sink
sI – Small Isolator


EXIT
BIOSAFETY LEVEL 3 AREA
DO NOT ENTER
CAUTION
CAUTION


CAUTION

Conclusion

Reverse genetics of NDV enabled

- Identification of molecular basis of pathogenicity (F, HN and V proteins)
- Development of improved vaccines
- Development of NDV-vectored vaccines