EADGENE
European Animal Disease Genomics Network of Excellence for Animal Health and Food Safety

Genomics for Animal Health: Outlook for the Future

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Emerging and re-emerging viruses

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ROSLIN

- 75% of new emerging diseases are RNA viruses
- 87 new viruses discovered between 1980 and 2005
- New technologies **will** discovery many more viruses
- Last few years, Lipkin lab (Columbia) ~200 new viruses!
- If every vertebrate has 20 endemic viruses 20 x 50,000 = 1M
- New viruses often emerge in wildlife and livestock, some are zoonotic or have the potential to be
- Rodent-borne & vector-borne infections are biggest threats

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Examples of emerging & re-emerging viruses

- Foot and mouth disease virus
- SARS virus
- Chikungunya virus
- Crimean-Congo hemorrhagic fever virus
- Marek's disease virus
- Salmonid alphavirus
- West Nile virus
- Rift Valley fever virus
- Ebola virus
- Bluetongue virus

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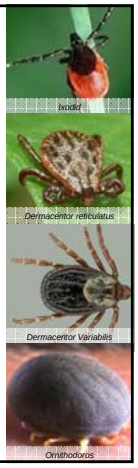
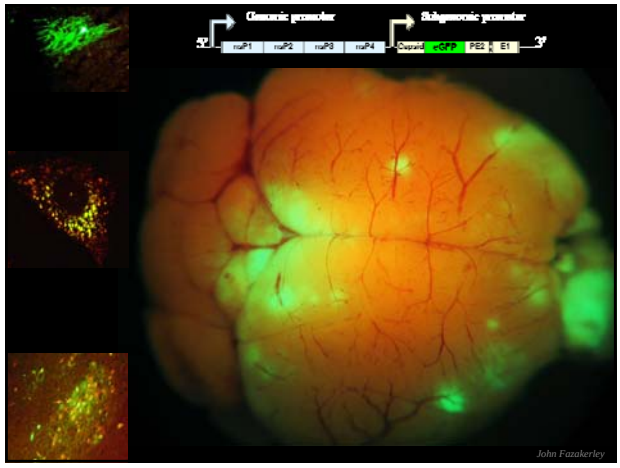
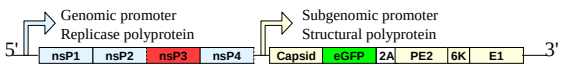
Arboviral diseases

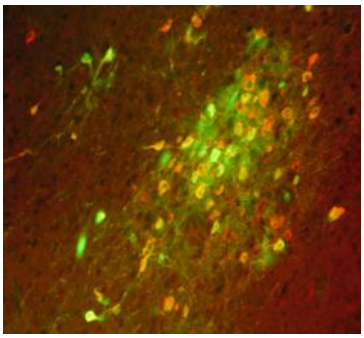
- Yellow fever
- Dengue (hgx) fever
- West Nile fever
- Murray Valley fever
- Japanese encephalitis virus
- Equine encephalitides
- Chikungunya
- Rift Valley fever
- Tick-borne encephalitis
- Crimean-Congo hgx fever
- Bluetongue







Focus of SFV infection in the cortex of a mouse brain



Fragkoudis et al., J. Neurovirol., 2008

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In mosquito cells, a phase of early rapid virus production is brought under control by the RNAi response giving rise to a persistent infection with low level virus production, no cell damage and no damage to the mosquito.

In vertebrate cells, infection induces cell stress, interferon and apoptosis. Clinical disease is most commonly asymptomatic, athralgia or encephalitis.

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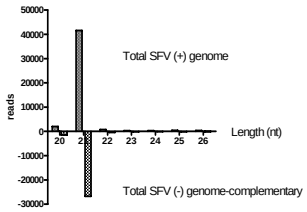
Population of small RNAs in SFV infected U4.4 cells

U4.4 cells infected with SFV4 (MOI = 10).
Total cellular RNA extracted at 24 h post-infection.
RNA population <44 bases (gel fractionation) sequenced by Illumina Solexa massive parallel sequencing, 4 M reads,
~2% of the small RNA population are virus derived.

Frequency of 20 to 26 nt RNA molecules



Aedes albopictus

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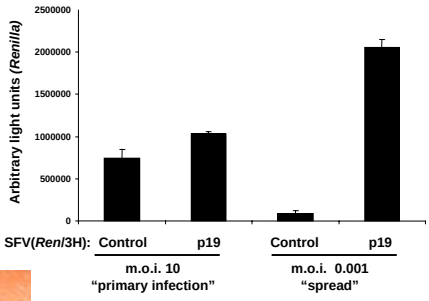
SFV P19 expression increases virus replication and spread



Aedes albopictus

U4.4 mosquito cells, 48 h post-infection

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Some factors contributing to increased threat in 21st century:

- (Better diagnosis and surveillance – perception)
- Increasing urbanisation/population increase
- Rapid and changing human mobility
- Changing human social practices
- Changing agricultural / land use practices
- Climate change
- Erosion of vector (eg mosquito) control programmes
- Spread of vectors (eg *Aedes albopictus,* Asian tiger mosquito to US, Brazil, Italy, Nigeria)
- Co-infections
- Inadequate surveillance
- Wars, bioterrorism and accidents

Emerging Infections

I. **Recognition of previously unrecognised disease**
Eg. California encephalitis – La Crosse virus
Sin Nombre, SARS, West Nile, Salmonid alphavirus, IBPV

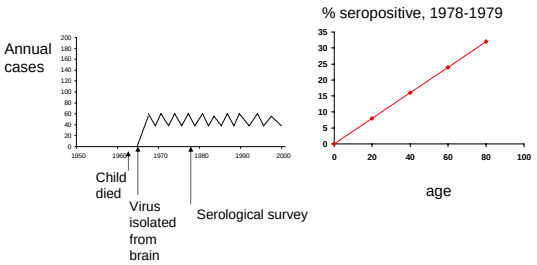
II. **Increase in ratio of cases to infections**
Eg. TB (host resistance, HIV)
Influenza (viral virulence), Marek's disease virus

III. **Increase in number of infections**
Eg. FMDV
Lassa, Ebola, HIV
Influenza
VEE, Rift Valley fever
BSE, vCJD

These are NOT mutually exclusive – provide a framework for thinking about the issue

I. Recognition of previously unrecognised disease

1. Improvements in clinical and diagnostic medicine



New diseases that are clinically unique, such as Hantavirus pulmonary syndrome and BSE, are more likely to be recognised **early** than diseases that closely resemble well-established clinical entities (diarrhoeas and pneumonias).

I. Recognition of previously unrecognised disease

2. Spillover into monitored population

Sin Nombre virus:

- Endemic in Western United States.
- Spread by deer mouse (*Peromyscus spp*).
- First recognised in 1993 because of the number and clustering of human cases.
- Increase in rodent numbers after two especially wet winters (increased availability of seeds of the pinon pine and other rodent food).
- Highlights potential effects of climate change

Others:

- Hendra / Nipah / SARS

I. Recognition of previously unrecognised disease

2. Spillover into monitored population

Severe Acute Respiratory Syndrome (SARS)

Started Feb 2002 Southern China, "ended" July 2003
China (incl Hong Kong), Taiwan, Canada, Singapore, Viet Nam
8,422 cases in 24 countries
916 cases fatal (11% case fatality rate)
Virus found in 'masked palm civet' (Paguma larvata)
Natural host is bats
Spread by respiratory droplets and fomites

I. Recognition of previously unrecognised disease

3. With reference to a specific geographical region

West Nile virus (USA, 1999)

Chikungunya virus (La Reunion, 2006)

Bluetongue virus (UK, 2008)

Rift Valley fever virus (Saudi Arabia/Yemen, 2000)

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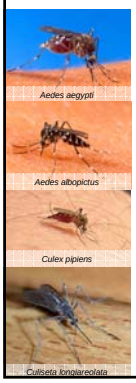
I. Recognition of previously unrecognised disease

3. With reference to a specific geographical region



Chikungunya

First described in Tanzania in 1950s.

2004, outbreak East Africa (*Aedes spp*).

2006, La Réunion Island, 266,000 cases (35% population; 22,000 in 1 week); 254 deaths.

2007, outbreak in Italy (*Ae albopictus*).

2008, now spread through islands of Indian Ocean into India and SE Asia, >5M infections.

Fever, rash, arthralgia, myalgia; differential diagnosis is dengue.

Complications: skin ulceration, deafness, ocular disease, myocarditis, hemorrhagic fever, encephalitis.

Could spread to N. Europe and USA.

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II. Increase in ratio of cases to infections

1. Host resistance can be altered without any change in virulence of the pathogen

Eg HIV and TB: About a third of the 33 million HIV-infected people worldwide are co-infected with Mycobacterium tuberculosis; 70% of these live in sub-Saharan Africa. HIV is the most powerful known risk factor for the reactivation of latent TB.

II. Increase in ratio of cases to infections

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2. The virus may increase in virulence without any change in host resistance. New variants (RNA variability). Recombination; reassortment; changes in tropism (receptor, intracellular factors); changes in pathogenesis (cytopathic effect, interaction with immune system).

   Eg, influenza (reassortment, changes in tropism, interaction with immune system), alphaviruses & enteroviruses (recombination); tick-borne encephalitis virus (changes in pathogenesis).

II. Increase in ratio of cases to infections

2. Increase in virus virulence

Influenza strains

Influenza well-recognised infections of birds, pigs, horses, humans and other spp.

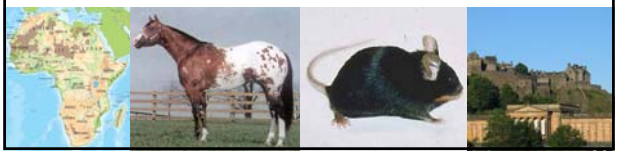
Since 2003, 442 cases of human H5N1, 262 have died

Marek's Disease virus

Increasingly virulent strains driven by vaccination

III. Increase in number of infections

1. Reinvasion of pathogen
2. Invasion across a species barrier
3. Increase in transmission rate



III. Increase in number of infections

1. Reinvasion

Measles:
Only infects humans
Requires a human population >500,000
Iceland: population of 250,000, striking periodic epidemics

Canine Distemper Iceland:
Usually absent from Iceland
Vaccination not used
Three epidemics 20th century; dogs not properly quarantined
Losses up to 90% of dog population

Canine Distemper Africa
1994, 2001, lions in Tanzania (Serengeti)

III. Increase in number of infections

2. Invasion across a species barrier
Eg HIV, zoonoses (arboviruses), BSE, Ebola, SARS.

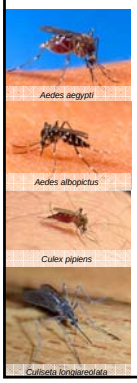
III. Increase in number of infections

3. Increase in transmission rate

Yellow Fever	Vector control measures
Dengue	Vector (spread of)
TBE	Vector (increasing numbers)
Sin Nombre	Vector
HIV	Social factors
Ebola	Travel
Hep C	Social factors
Norovirus	Social factors
BSE	Agricultural practices
Bluetongue	Climate?
CCHF	Wars / land use

III. Increase in number of infections

3. Increase in transmission rate



Venezuelan equine encephalitis virus

Endemic in tropical and subtropical forests & swamps (N, C and S America) - sporadic human disease.

Epizootics: >10,000 human
>100,000 equine cases

Illness in horses, burros, goats and dogs.

Epizootic viruses have small genetic changes.

Suitable mosquitoes and equines (amplifying hosts) are required for an epizootic.

1995,Venezuela and Columbia: >85,000 human cases, 3,000 neurological symptoms.

Surveillance and prevention

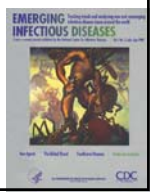
International: World Health Organisation (WHO)
Office Internationale epizooties (OIE)

National: Centre for Disease Control (CDC, USA)
Health Protection Agency (HPA, UK)

International / National reference Laboratories (flu, measles)

Rapid response teams (eg USAMRIID, CDC, WHO)

Emergency planning (International and National): meetings (eg flu), bioterrorism (smallpox), threats (FMFV)



Regulations: Imports and exports / quarantine

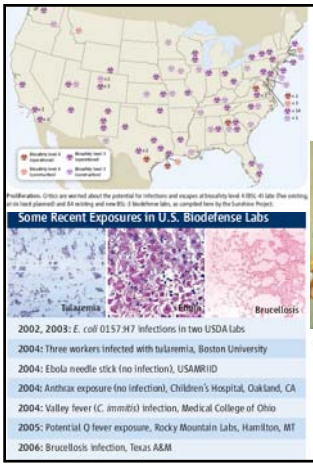
Isolation and diagnostics facilities

Vaccines (campaigns and stockpiles)

Therapeutics (eg antibiotics and antiviral)

Transmissible diseases with potential for very serious and rapid spread, irrespective of national borders, that are of serious socio-economic or public health consequence and that are of major importance in the international trade of animals and animal products are classified by the OIE as 'list A' pathogens.

Foot and mouth disease	Vesicular stomatitis
Swine vesicular disease	Rinderpest
Peste des petits ruminants	Contagious bovine pleuropneumonia
Lumpy skin disease	Rift Valley fever
Bluetongue	Sheep pox and goat pox
African horse sickness	African swine fever
Classical swine fever	Highly pathogenic avian influenza
Newcastle disease	



Accidents

There are now 20,000 people at 400 sites around the US working with putative bioweapons, 10 times more than before 9/11

Plague of bioweapons accidents afflicts the US, NewScientist.com news service, 05 July 2007

2008, FMDV – Pirbright UK

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