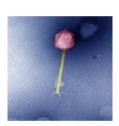


Nancy Holroyd

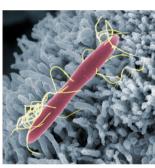
Introduction to Infectious Diseases Seminar Series

March 15th 2011

Infectious diseases – all shapes & sizes



Phage Image David Goulding



Clostridium difficile – 'bad guy' Image David Goulding



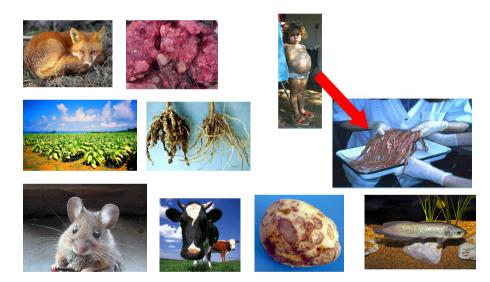
Worms - helminths

Helminths are parasitic worms...





...that parasitise many host species



Tree of life



Roundworms (nematodes)



Ascaris lumbricoides (roundworm)



Necator ancylostoma (hookworm)



Strongyloides ratti (threadworn

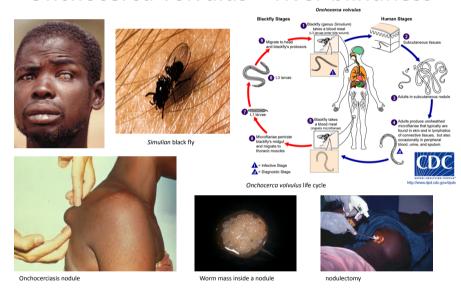


Trichuris (whipworm)

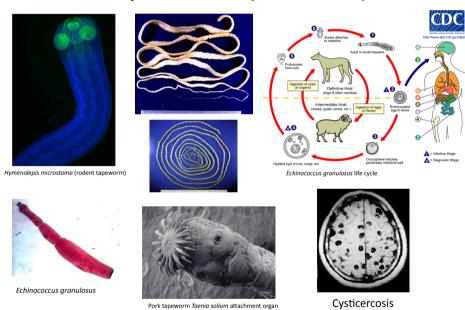


Trichuris (whipworm)

Onchocerca volvulus – river blindness



Tapeworms (cestodes)



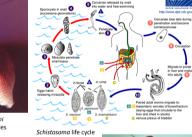
Flukes (Trematodes)



Schistosoma mansoni cercaria

Schistosoma mansoni adult male and females







Clinical manifesation o schistosomiasis





History of helminths



Why are helminths important today?



1st WHO report on Neglected Tropical Diseases, 2010

Buruli Ulcer Leprosy

Chagas disease (American trypanosomiasis) Lymphatic filariasis

Cysticercosis Onchocerciasis

Dengue haemorrhagic fever Rabies

Dranunculiasis (guinea worm disease) Schistosomiasis

Echinococcosis Soil transmitted helminthiasis

Fascioliasis Snakebite

Human African trypanosomiasis Trachoma

Leishmaniasis Yaws

Neglected Tropical Diseases (NTD)

...primarily infectious diseases.



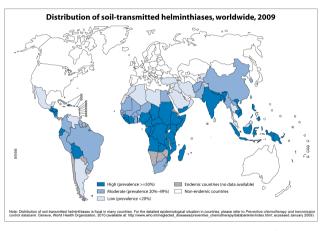
...thrive in impoverished settings, especially tropical climates.

...[mostly] parasitic diseases, spread by insects... and snails ... [or] spread by contaminated water and soil infested with the eggs of worms.

...transmission cycles... perpetuated by poor standards of living and hygiene.

...concentrated in settings of extreme poverty.

Where does helminthiases occur?

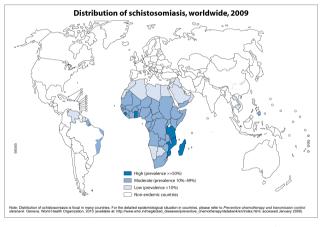


The columbrates allow makes shown and are designations as also do it as imput on the imply the expression of any opinion whatsoever on the part of the Whorld Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not vet be full agreement, 40 WHO 2010. All rights reserved

Data Source: World Health Organizati Map Production: Control of Neglected Tropical Diseases (NTD) World Health Organization



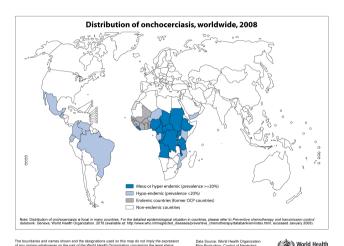
Where does schistosomiasis occur?



The boundaries and names shown and the designations used on this map do not imply the expres if any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontier to boundaries. Dotted lines on maps represent approximate border lines for which there may not with full surrelement. Or WHO 2010. All rights research. Data Source: World Health Organiza Map Production: Control of Neglecta Tropical Diseases (NTD) World Health Organization



Where does onchocerciasis occur?



Disease characteristics







Dranunculus

Lymphatic filariasis







River blindness

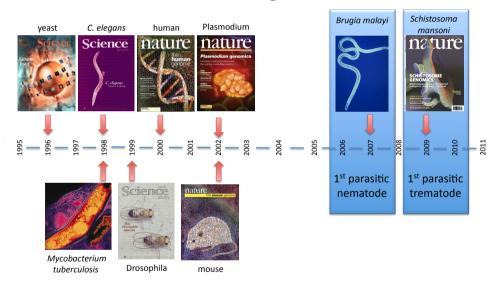
Global burden of infectious disease

| | Disease | Morbity, | Deaths |
|-----------|----------------------|-------------------------|---------|
| | | DALYs* | (1000s) |
| | | (millions) | |
| Viral | HIV-AIDS | 84.5 | 2,600 |
| Bacterial | Tuberculosis | 34.7- 46.5a | 1,600 |
| Protozoa | Malaria | 35.7ª - 46.5 | 1,300 |
| Helminths | Schistosomiasis | 4.5 - >18 ^b | 280 |
| | Hookworm | 0.1 - 22.1 ^a | 65 |
| | Ascariasis | 1.8 - 10.5 ^a | 60 |
| | Trichuriasis | 1.0 - 6.4a | 10 |
| | Lymphatic filariasis | 5.8 | |
| | Onchocerciasis | 0.5 | |

* Disability adjusted life years.

Source: World Health Report (2004) WHO. Except for: ^a Chan (1997) Parasitol. Today; ^b King et al (2005) Lancet

Helminths & genomics



WTSI helminth genomes



http://www.sanger.ac.uk/resources/downloads/helminths/

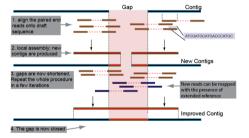
Challenges we're tackling

- De novo sequencing
- Source DNA
 - Scarce
 - Variable
- Long range information (DNA hungry)

WTSI's niche in helminth genomics

- High quality reference genomes
- Automated & manual improvement





Tsai et al. (2010) Genome Biology

<u>ICORN</u> – Iterative Correction of Reference Nucleotides

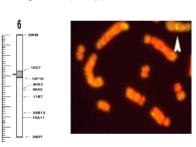


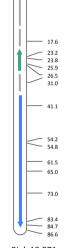
Otto et al. (2010) Bioinformatics

Schistosoma mansoni

- Initial draft published in 2009
 - survey of gene content
 - was 51,000 contigs ... New draft now 9,000 (N50 16 -> 78 kb)
 - was 19,000 scaffolds ...New draft now 570 (N50 0.8 -> 32 Mb)
- Latest: 174 scaffolds (81% of genome) mapped to chromosomes*





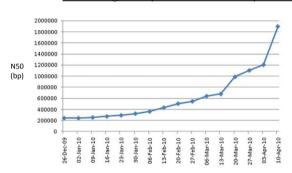


*using linkage map from Criscione et al (2009) Genome Biol. 10:R71.

Echinococcus multilocularis



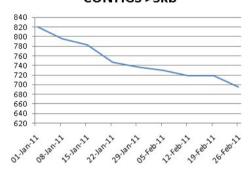
N50 throughout 'sprint 1' of manual improvement



Echinococcus multilocularis



CONTIGS >5kb



Worm therapy



Auto-immune protection



DIY worm therapy

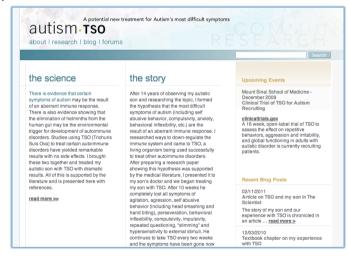
Latrine walking in Cameroon





DIY worm therapy

Whipworm treatment of autism



Parasitic helminths

- Hugely diverse group.
- Medical & economical impact for billions of people, particularly in developing countries.
- Key reference genomes from Sanger will accelerate research into these organisms.

Acknowledgements

Parasite Genomics group

Matt Berriman

James Cotton

Bernardo Foth

Taisei Kikuchi

Antonio Murio

Anna Protasio

Alejandro Sanchez

Magdalena Zarowiecki

Adam Reid

Jason Tsai

Thomas dan Otto

Helminth finishing teams

SA

Richard Clark
Christine Lloyd

ne Lioya 454 se

Anna Babbage

Helen Beasley

Karen Brooks

Karen Holt

Sarah Nichol

David Saunders

Kathy Seeger

Christopher Stephens

Alan Tracey

Sequencing Division

SAGE teams

454 sequencing

Library construction

Illumina sequencing

PSD

+ lots more people at WTSI

& our collaborators around

the world.

Helminth Morphology

| Cestodes | Trematodes | Nematodes |
|-----------------------------------|-------------------------------|---------------------------------------------------------------------|
| flatworm, segmented | flatworm, non- segmented | round worms |
| e.g. tapeworms (pork tapeworm) | e.g. flukes (Schistosomes) | e.g. major intestinal worms, filarial worms (river blindness) |
| hermaphrodite | hermaphrodite or dioecious | male & female |
| no digestive tube | digestive tract to caecum | digestive tract to anus |
| oral sucker | oral sucker | lips and teeth |