Unit 1

What is the natural history for HIV - Immunity compromising parasite that causes AIDS(occurs when immune system fails, too few CD4, opportunistic infections by pathogens that are usually not harmful), retroviruses that make DNA in host - Has geographically distributed infection patterns that show adaption and diversity - Across the world it is number 4 cause of death, 84M infections 40M deaths (covid is 600M + 6M), most prev in sub-Saharan Africa (23.5M) it decreases away from the eq. - The pattern since 1990s has been to increase then level off recently o In south Africa the life expectancy at birth decreased to levels unseen since 1960s (n shape), number of people newly infected each year has been decreasing esp since 200s as we started to understand it

How HIV infects a cell 1. HIV virion has RNA genome with integrase, protease, RT inside, gp41 anchor protein with gp120 surface protein 2. Binds to CD4, corecepto-r,CCR5 on human cell and fuses 3. RT creates DNA which is spliced into host by integrase, making it transcribe HIV mRNA and create new HIV proteins which assemble and bud off, then mature into new virion

Unit 1 (cont)

Mode of transm-ission is region dependent - Likely mode of transm-ission is mainly hetero-sexual sex or injection in indo, kenya, Russia but MM sex in US and canada (hetero in uk!)

Immune system response - Dendrite captures virus and activates naïve helper T, these produce effector helper T (some also become memory helper T cells) - Effectors stimulate B cells which make antibodies that inactivate the virus, also activate killer T which destroy hosts who have the virus - But macrophage, effectors and memory Ts have CD4 and CCR5 which makes them targets for HIV

Unit 1 (cont)

We have become complacent - Huge increase in infections in MM in USA in 84, shot down in 1987 with drugs but increasing slowly as we are complacent

HIV load - Virions Acute(0-12): sharp increase then decrease as immune fights Chronic(1yr-7): levels off as they infect t cells AIDs: sharp increase again - CD4 Tcells, acute: sharp decrease as they fight chronic:increase in blood at start but then slowly goes down until it hits AIDS:2-00cells/mm3

Unit 1 (cont)

Where and when did HIV originate - HIV can evolve in one person and then an ancestor goes to the next patient, new enviro=new evo, we can build an accurate diagram with some parts! - HIV-1 was transfected from chimps to people many times HIV-2 was from monkeys o HIV2 is not as transmissible or fatal and didn't cause the epidemic, group M HIV1 is the most prevalent strain and our species had no T to deal with it - HIV evolves rapidly which makes vax hard - To estimate the time we had to guess the starting point, used unrooted phenogram, genetic differences and linear regression (molecular clock) 159 strains and do pairwise comparison, estimate divergence from common ancestor and extrapolate (back to 1914-1915)

Affects on body - Chronic infection damaged lymp leading to less T, HIV depletes CD4+ T in gut damaging it, allows bacteria into blood, bacteria in blood induces immune system which causes T cell prolif, giving HIV more cells to target (it does best in activated CD4+ Ts)

Unit 1 (cont)

Are human populations evolving - Greatest resistance is in Scandinavia and deceases as you move to Africa - Some individuals have mutant CCR5-delta32 allele which is mutant CCR5 that hiv cannot bind too, probably not the cause of lack of virus here though, we could not have evolved this fast - The cost is being more likely to contract west nile virus (in another enviro it would be bad!) - We are 2 nucleotides away from HIV resistance, likely this one was genetic drift from viking hoards - We also have CD4 and most people have C868 (gives arginine) but some have T which gives tryptophan, this mutation causes them to contract HIV faster

Why did single drug therapies fail AZT - Developed within 5 years, very promising, AZT is added instead of Thymine DNA to DNA by RT, less likely in mutants with RT errors, will add DNA Thymie with amide which stops the chain - Population inside will evolve within about 6 months, need to keep increasing the concentration, new RT will add it but then correct the mistake and remove it (likely still added though) - Natural selection occurs as there is a population inside an individual with mutations, when the population changes (AZT intro), resistant virions become the most fit (before they were less fit) could go back, natural selection is enviro and reversible o Changed to genetic makeup in HIV pop over time led to increased drug resistance, virions with heritable traits conferred enhanced fitness ✉ greater proportion in HIV populations

bio sheet2 Cheat Sheet

by bioevocrib via cheatography.com/166342/cs/34819/

Unit 1 (cont)

Why are infections fatal - Not intuitive, generally HIV evolves to be more aggressive and virulent over time, comp fitness increases then levels off, short sighted because host will die - We see more virulent means less time until aids, greater virulence over time too (more transmissible), overall transmission is max right in the middle (fits with fraction of patients with viral loads too) - As rate of mutation increases time to aids decreases, response by host can contribute to fatality (t cells in response helps viral proliferation) - Sometimes HIV virons produce variants the immune system can't recognize, we can display p24 or HLA, in patients with HLA-B alleles the mutations to TSN makes it less detectable than the original TST in virus epitope - HIV can also bind to CXCR4 coreceptor and these viruses evolves faster to kill more T progressing to aids faster, more transmissible as they get more lethal Unit 2 – support for evolution

HAART - Highly active antiretroviral therapy (3+ drugs), increased survival, takes longer to evolve resistance to multiple drugs - Risk of evolving HIV resistance increases when you have done 80-90 prescriptions, many stop here because side effect is so bad ✉ resistant populations

unit 2

Pattern – fact or observation (cladogram)+ process – inferred mechanism (phylogenetic tree)=theory - Anaximander first thought humans came from something simple into complex - Empedocles thought poorly adapted species die (extinction!) - Artistotle "scala naturae" throught there was a linear scale of species that was fixed and independent… halted evolution for year

Observers - Comte de buffon, Erasmus Darwin, jean-baptiste Lamarck, Robert chambers Mechanisms - William Charles wells, Patrick matthew, Alfred Russell Wallace

unit 2 (cont)

Selective lab breeding with mice (MICRO change over time) - High runners from each fam, selected for physical ability as they ran longer and faster against control Natural populations(MICRO) - Three types of flower, one late flowering and one early, crossed and got middle! Vestigial structures(MICRO) - Kiwi reduced wings, limbs in vertebrates, tail bones (coccyx) and arrector pili in humans - Can also be genetic: we have a gene (CMAH 92bp) that creates an enzume with no function from chimps (incomplete sugar coversion but grants malaria resistance!) - Developmental: chicks digits are homologous to ours when developing then they lose 1 Lab and natural experiments(speciation: new from old) - Lab flies feeding on starch vs maltose for a year, virgins preferred own diet flies - Warblers have to go around tiberan plateau, larger distance to travel will be more different when they meet, genetic diff and song diff, change occurs!

Extinction (MACRO new forms from old) - Irish elk, giant deer who went extinct Succession - Extant form is a succession of fossil form before it (slight changes) Transitional forms - Archeopteryx, link between dinos and birds this helped as more evidence for evolution - Turtle shells - Ribs expand outside shoulder blades to form shell, amniotes should have ribes inside, we have a transitional form - Leeping blenny (terrestrial fish) infer aquatic then see transition to amphib, then terrestrial

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unit 2 (cont)

Evolutionary branching diagram pattern from analysis (cladogram) vs evolutionary tree is genealogical relationships inferred from evolution (phylogenetic tree) - We can use homologous traits to test shared ancestory, they should share a set of nested traits, also show trait appearance order

Apomorphy: derived trait separate to ancestral Plesiomorphy: ancestral trait, synapomorphy: derived trait by 2+ lineages Homology: can be mol, dev, structural but must be representable as single synapomoprhic

unit 2 (cont)

Geological time scale – Early is likely 148,000,000 (based on Pangaea drift, how long to get gap) Uniformitatianism: Processes from past continue today Superposition: New material goes on top Original horizontality: Originally laid down horizontally Cross cutting relationships: Upper layer are younger Inclusions: Inclusions are older than host Faunal succession: extant resembles extinct - Eras aren't even because it is based on mass extinctions usually, red dots are the minimal divergence year

Ex. Shared dervived molecular trait, PMP-22 locus on chromo 17, CMT1A is on both sides leading to unequal crossing can lead to neuropathy and Charcot marie tooth disease 1A, shared in chimps and humans Ex. Shared loss, pseudogenes of only exons are shared most with closest related ancestors Ex. Shared derived developmental traits like pharyngeal pouches (gills in fish) and tail in fetus Ex. Shared derived structural trait: vertebrate forelimbs and orchid elements **Homoplasy: cannot represent as synapomorphic trait, must have evolved separately**

unit 2 (cont)

Can now use radiometric dating, if we know the decay rate we should be able to get the time Nt=N(0)e^-lamda(decay rate)xt - Can use Ar-40 and c-14 to get the entire range of the earth (100-4.5bil) Special creation: religious doctrine, species do not change or split, they appeared recently

Unit 3

4 postulates, 1. Variation among ind for some trait, 2. Trait properties are heritable, 3. Individuals compete for limited resources, 3. Skewed survival and reproduction, some are more successful

Fitness: typical individuals ability to survive and reproduce in its environment (can be better to have bigger kids than many small ones so not just the number, not just the ind!) Adaptation: microevolutionary, trit that increases organisms fitness relative to others - Humans can mess this up but we can see in bee visits and female function flowers inc next gen by being more fit

Unit 3 (cont)

Darwin's finches (he rarely said finch or evolution in first addition)/Grant's finches - Captured and tagged medium ground finch on daphne major, showed variation in beak depth (1), that beaks correlated in parents and offspring (2), individuals competed for food (3) only large food was left so only those who ate it survived survival and repro was skewed (4), changed pop into large bird with large beaks o (2) Specifically Bmp4 mRNA differs in embryos, more means larger beak depth Natural selection operates at the individual and phenotypic level in past and present but produces changes at the population and genotypic level (average moves), cannot operate FOR the future, operates on existing traits but may yield new ones (ex corn kernel inc into new species) - Evolution is a historical science but preadaptation is wrong, they are random, we use exaptation instead (new use or had no use but is now an adaptation) ex. Panda thumbs due to malformed wrist, this actually outcompeted! - Natural selection may yield many adaptations none of which can be perfect ex. NOT gono! finch beaks are wide as well, not perfectly deep and narrow - Natural selection is not exactly random, biased to those with best traits but operates on random variation - Survival of fittest, this is circular, we just see if 4 postulates and say evolution should eveolve - Macro and micro (species shall not beget species if you are cladist)

Unit 3 (cont)

Fitness: measured via survival and offspring (lineage), selection: measures in proportional repro Problems with Darwinism - He did not have the correct mechanism for inheritance, nothing for variation, thought the earth was only 15,000,000 which was not enough time - Believed in blending but this would never be able to produce light coloured ind from blended parents, but even heterozygotes can be pale (arg151cys mutation doesn't let MSH in to phenomelanin), agouti signalling also causes blockage

Modern synthesis: fisher,haldane,Dobzhansky,wright,Huxley,mayr,Simpson,Stebbins - Neodarwin postulates: mutation seg and ind assortment produce variation (1), transmit alleles (2), ind compete(3) leading to skewed survival (4) Epigenetics: Waddington 1942 to describe geneXenviroment, later assoc with spatial and temporal activity, now with cellular changes in gene function Intelligent design: special creation, must be a god making it, not really, if we build modules we can get it faster, Darwin's eye works like this (can see step before and look at history), inherit from ancestor ex. Crystallin proteins, lactate is redone to be used in our eyes