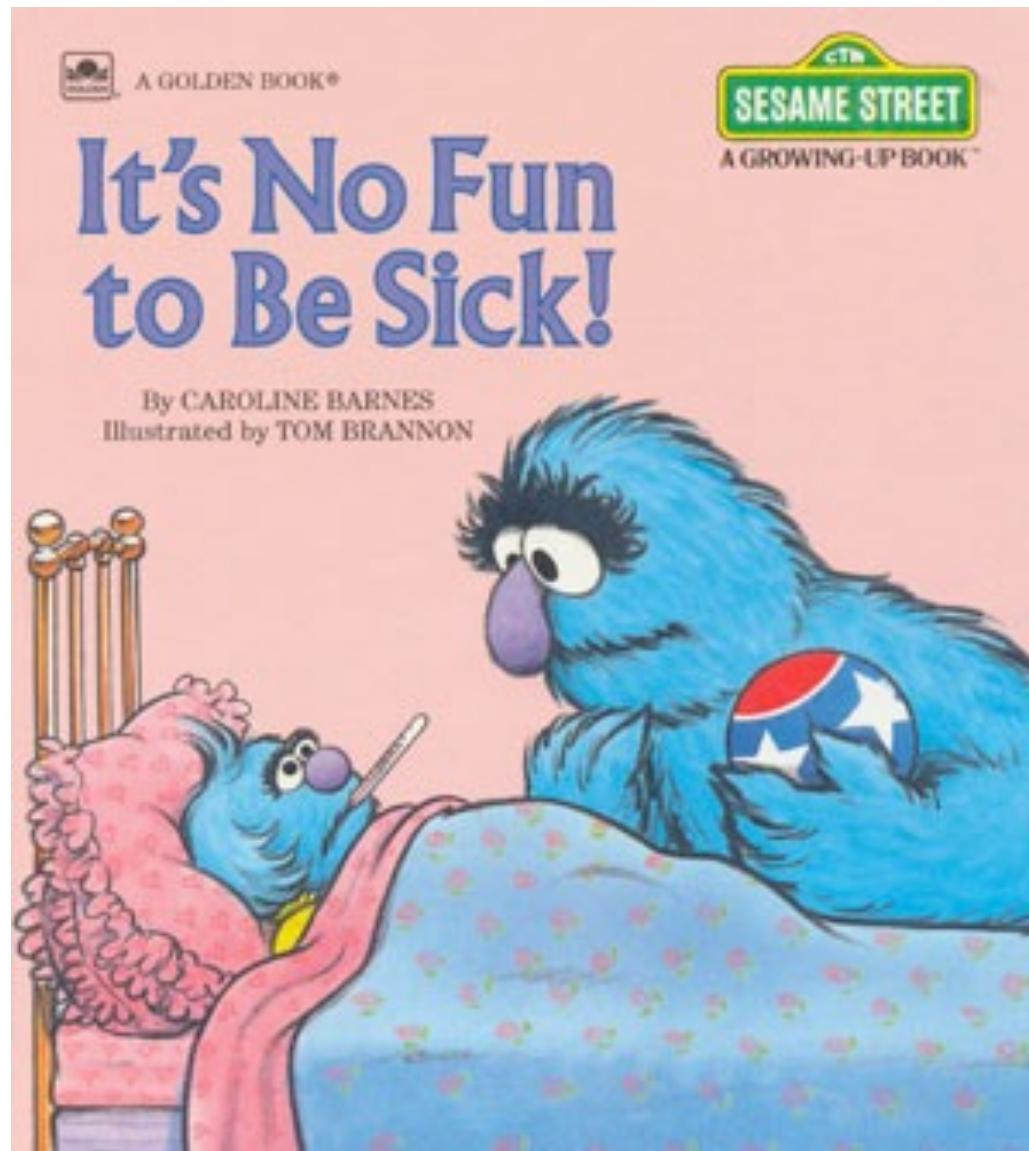
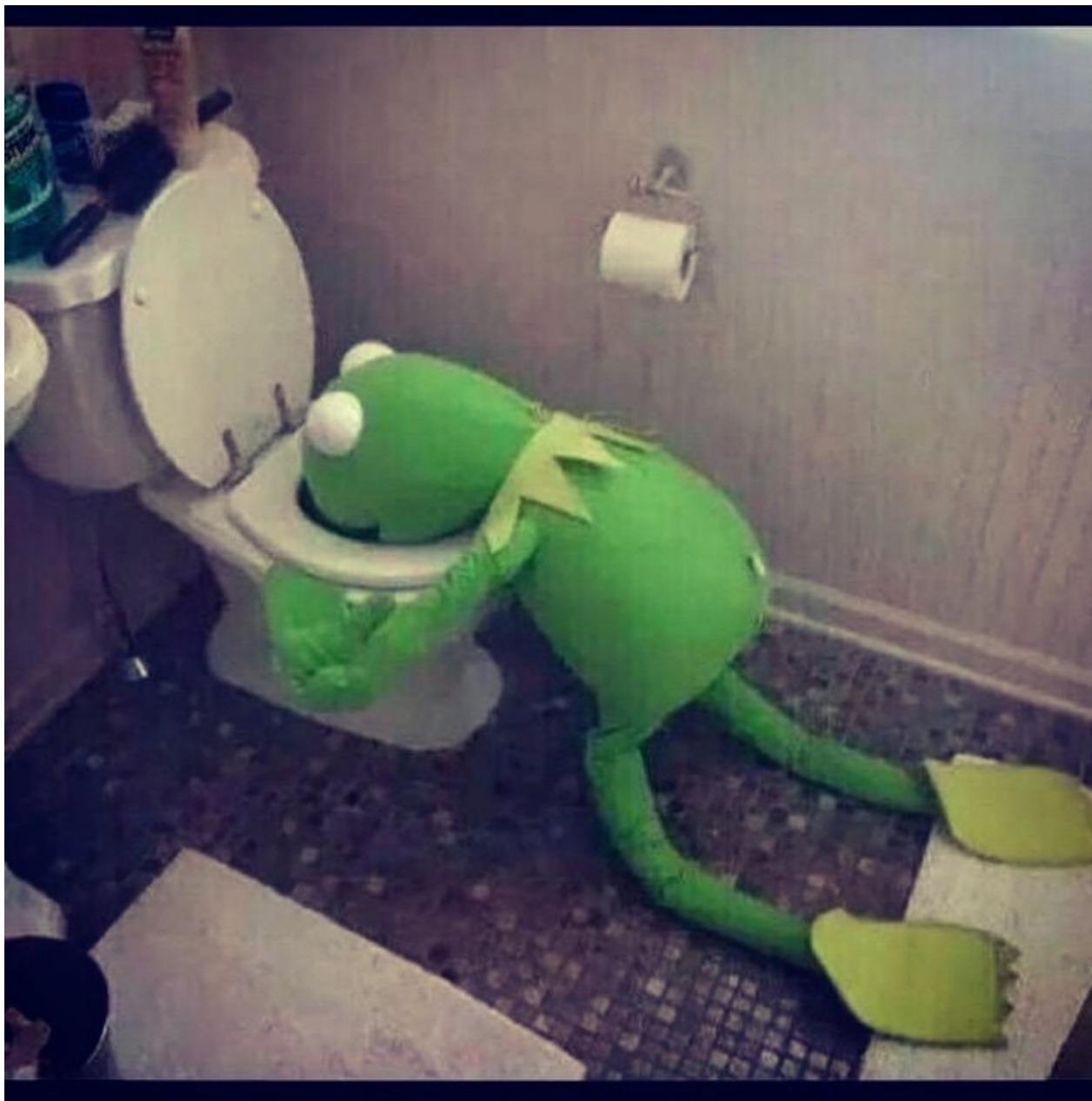


# HOST POPULATION GENOMIC APPLICATIONS IN DISEASE



# HOST POPULATION GENOMIC APPLICATIONS IN DISEASE



# OUTLINE

(ME TALKING: ~20 MINS)

- I. MOLECULAR APPROACHES FOR POPULATION GENOMICS
- II. HOST LANDSCAPE GENOMIC APPROACHES
- III. HOST DISEASE RESISTANCE
- IV. HOST INBREEDING DEPRESSION-DISEASE INTERACTIONS

(YOU THINKING, US DISCUSSING: ~20 MINS)

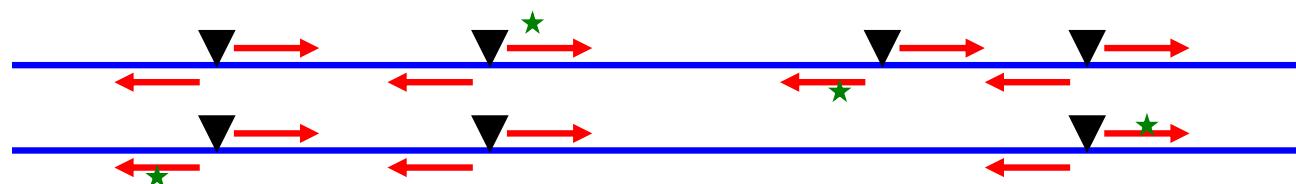
- V. PAIRS: “FLASH” HOST POP GENOMICS RESEARCH DESIGN
- VI. GROUP DISCUSSION OF RESEARCH IDEAS

# POPULATION GENOMIC APPROACHES

Method name	Brief description
Whole-genome sequencing (WGS; Pritchard 2011)	Sequencing of the entire genome, usually using shotgun sequencing. Can range from development of an annotated reference genome using high coverage to resequencing at low depth.
Restriction site-associated DNA sequencing (RAD-seq; Andrews <i>et al.</i> 2016)	A suite of reduced representation methods that sequence and genotype loci adjacent to restriction sites
Targeted capture (Jones & Good 2016)	A reduced representation method that enriches for targeted regions of the genome using labeled oligonucleotides
Ultraconserved elements (UCE; Faircloth <i>et al.</i> 2012)	Highly conserved regions of the genome that can be used to generate sequence data at orthologous loci from evolutionarily distant taxa
Anchored phylogenomics (Lemmon <i>et al.</i> 2012)	Sequencing and genotyping of libraries enriched for UCEs, anonymous, and/or functional loci
Transcriptomics (e.g., RNA-seq; Wang <i>et al.</i> 2009)	Analysis of gene expression levels, usually conducted by sequencing cDNA from RNA (RNA-seq)

# Genomic Tools

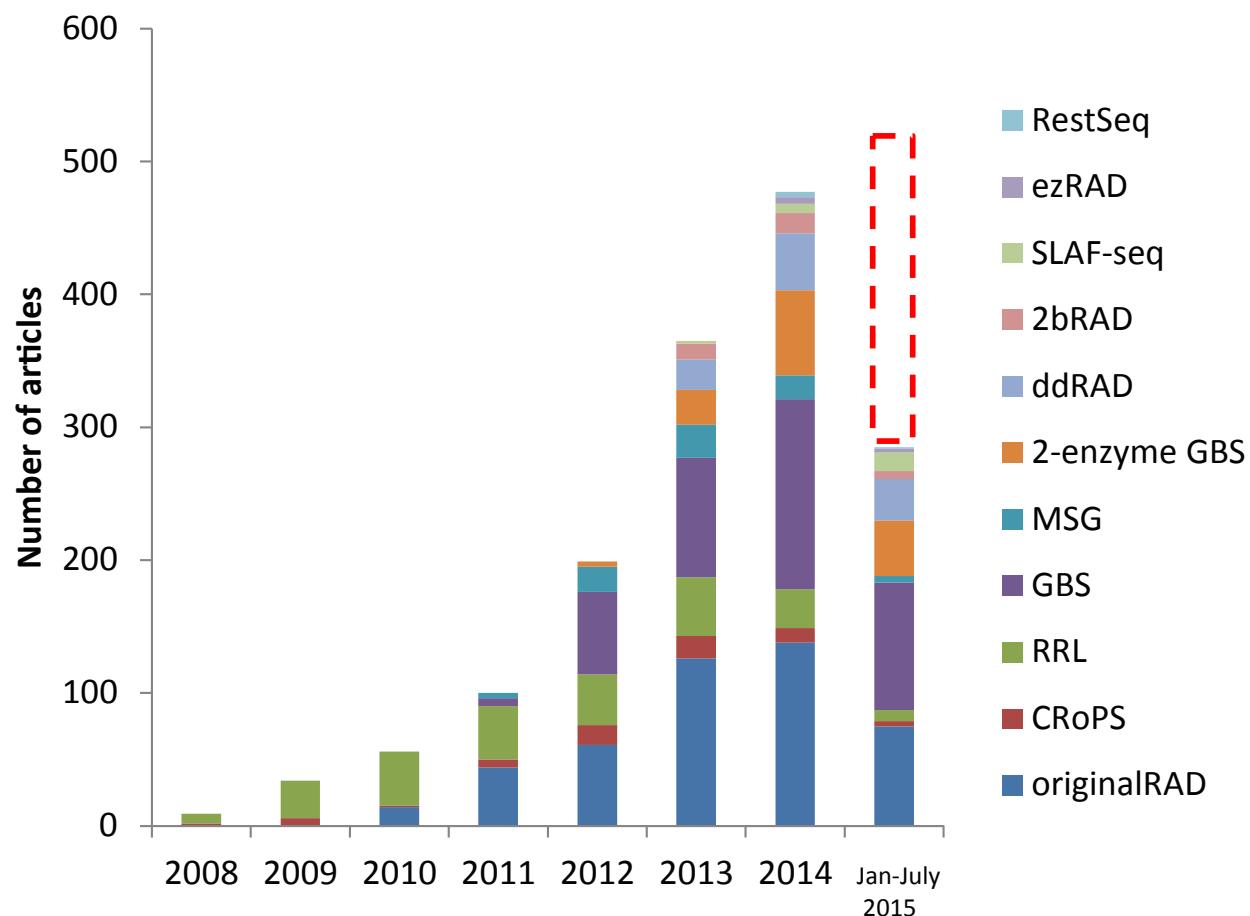
- Whole-genome resequencing
- Transcriptome sequencing
- Targeted sequencing
  - Exon capture
- Anonymous genomic sequencing
  - Restriction enzyme-based methods (RAD sequencing)



Davey et al (2011) *Nat Rev Genet* 12:499  
Andrews et al (2016) *Nat Rev Genet* 17:81

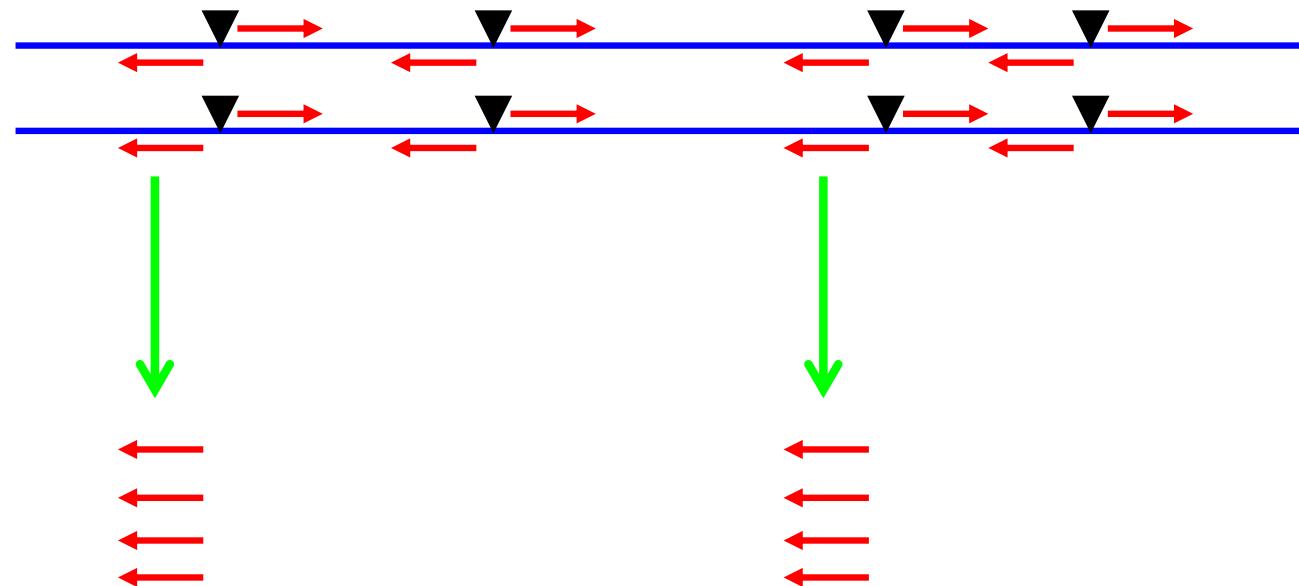
# Harnessing the power of RADseq for ecological and evolutionary genomics

Kimberly R. Andrews<sup>1</sup>, Jeffrey M. Good<sup>2</sup>, Michael R. Miller<sup>3</sup>, Gordon Luikart<sup>4</sup>  
and Paul A. Hohenlohe<sup>5</sup>



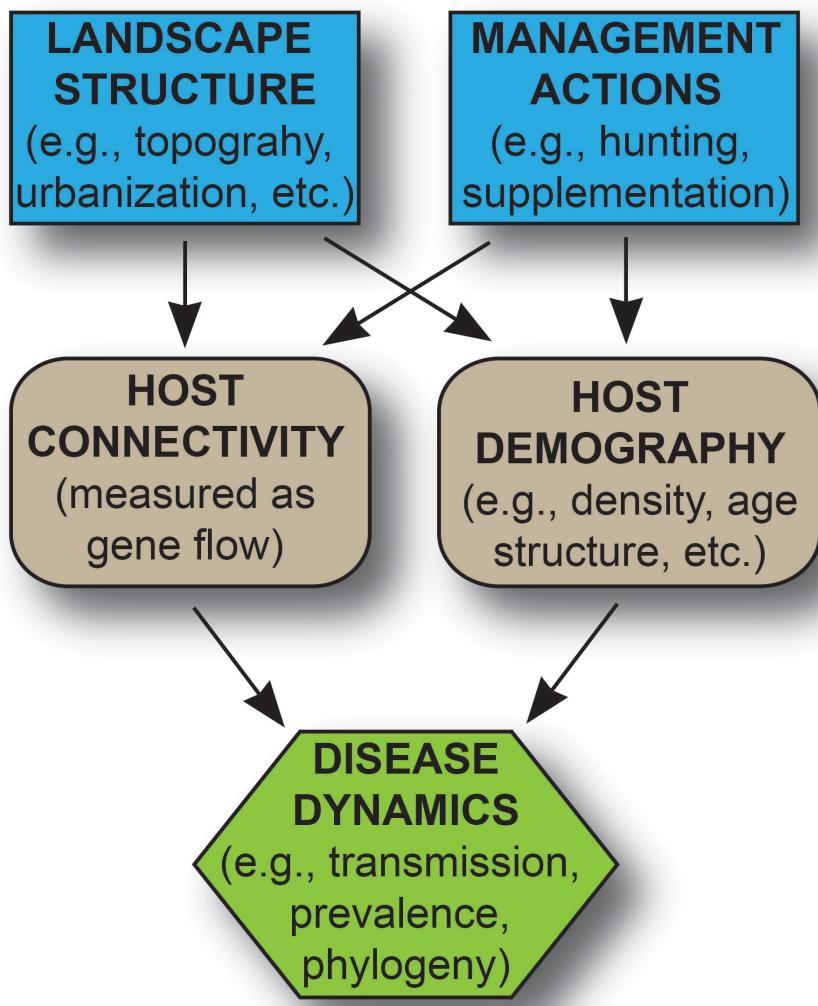
# Genetics of disease phenotypes

- RAD + capture = Rapture (Ali et al 2016 Genetics 202:389)

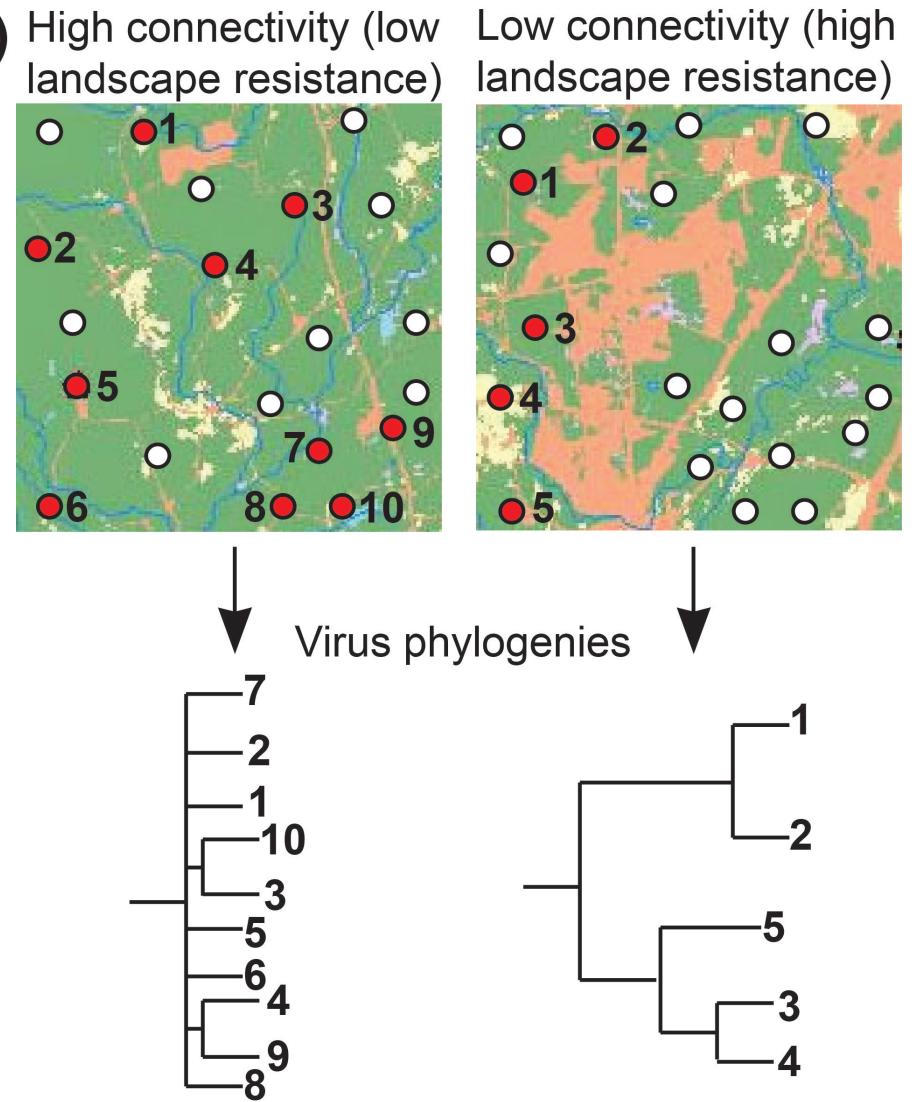


# LANDSCAPE GENOMICS: GENERAL IDEA

(A)



(B)



# LANDSCAPE GENOMICS: HOST CONNECTIVITY EXAMPLE

## MOLECULAR ECOLOGY

Molecular Ecology (2010) 19, 3515–3531

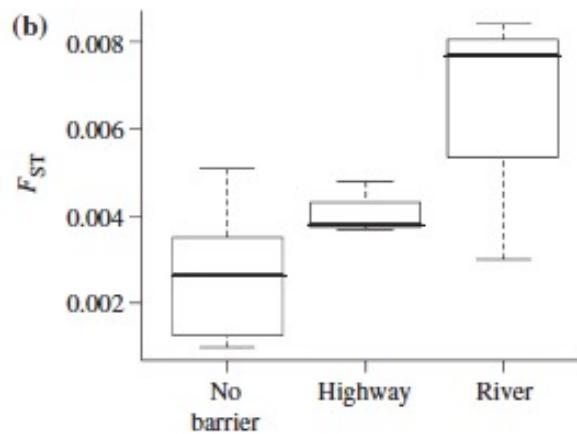
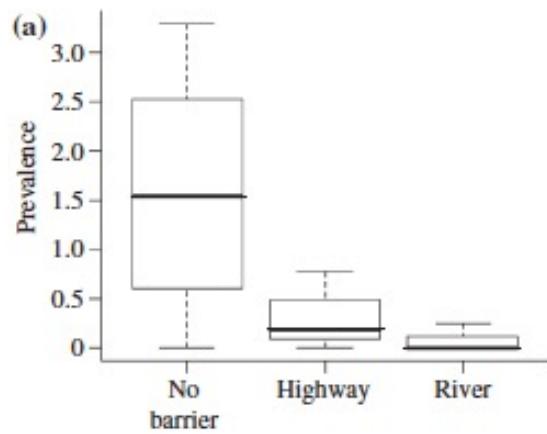
doi: 10.1111/j.1365-294X.2010.04679.x

### The landscape genetics of infectious disease emergence and spread

ROMAN BIEK\* and LESLIE A. REAL†‡

\*Division of Ecology and Evolutionary Biology, Boyd Orr Centre for Population and Ecosystem Health, University of Glasgow, Glasgow G12 8QQ, UK, †Department of Biology, Center for Disease Ecology, Emory University, 1510 Clifton Road, Atlanta, GA 30322, USA, ‡Fogarty International Center, National Institutes of Health, Bethesda, MD 20892, USA

# LANDSCAPE GENOMICS: HOST CONNECTIVITY EXAMPLE



**Fig. 1** Chronic wasting disease (CWD) in white-tailed deer as an example of using host population genetics to identify landscape determinants of disease spread. (a) Prevalence of CWD in 15 study areas in Wisconsin and (b) genetic differentiation ( $F_{ST}$ ) of deer host populations in study areas relative to core area of CWD infection, with study areas grouped based on the type of landscape feature separating them from the core area. Reprinted from Blanchong *et al.* (2008) with permission.

# LANDSCAPE GENOMICS: DIVERGENT SELECTION EXAMPLE

## MOLECULAR ECOLOGY

Molecular Ecology (2016) 25, 324–341

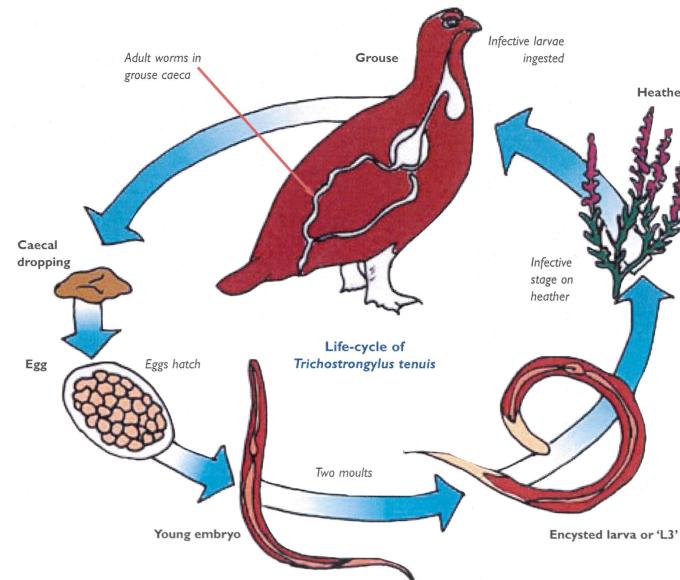
doi: 10.1111/mec.13473

### DETECTING SELECTION IN NATURAL POPULATIONS: MAKING SENSE OF GENOME SCANS AND TOWARDS ALTERNATIVE SOLUTIONS

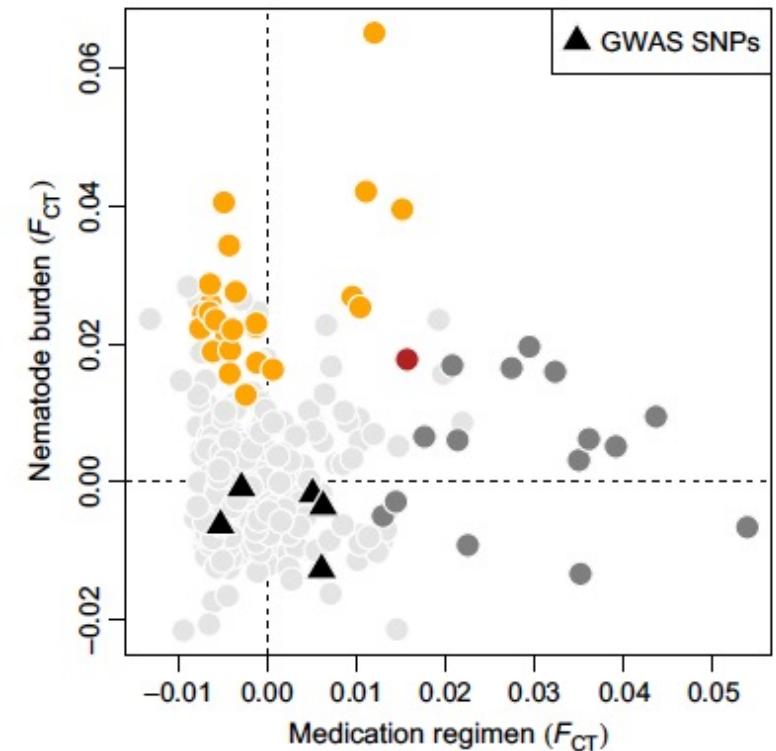
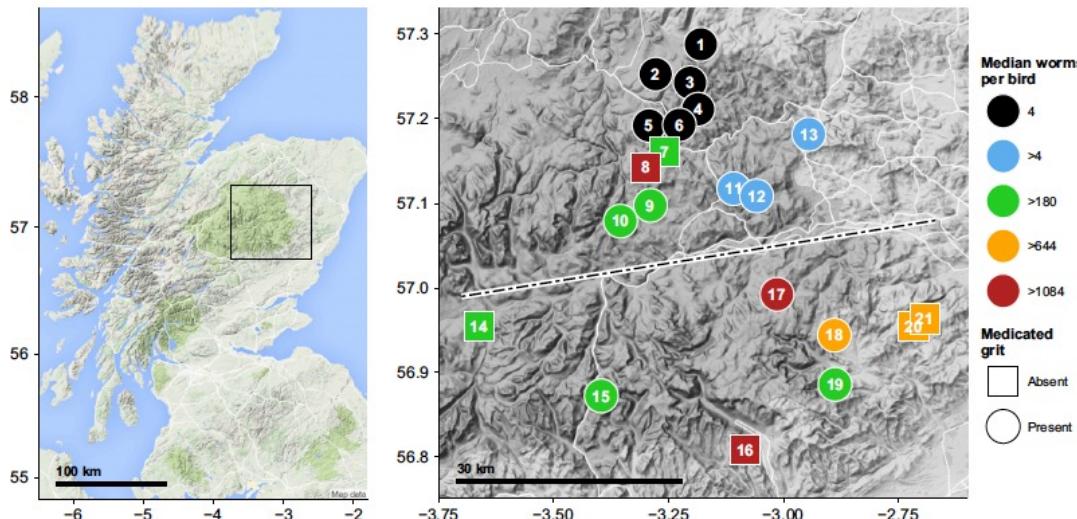
### The role of parasite-driven selection in shaping landscape genomic structure in red grouse (*Lagopus lagopus scotica*)

MARIUS A. WENZEL, ALEX DOUGLAS, MARIANNE C. JAMES,<sup>1</sup> STEVE M. REDPATH and STUART B. PIERTNEY

Institute of Biological and Environmental Sciences, University of Aberdeen, Tillydrone Avenue, Aberdeen AB24 2TZ, UK



# LANDSCAPE GENOMICS: DIVERGENT SELECTION EXAMPLE



**Fig. 2** Graphical summary of SNP-by-SNP hierarchical AMOVA testing for genetic differentiation among populations grouped by median nematode burden or anthelmintic medication regimen. Each data point represents the degree of genetic differentiation among population groups ( $F_{CT}$ ) at a single SNP. Statistically significant  $F_{CT}$  estimates (single-test  $P \leq 0.05$ ) are colour-coded (dark grey: medication regimen; orange: nematode burden; red: both; all SNPs not significant with FDR-corrected  $q > 0.1$ ). Five candidate SNPs for nematode-driven selection previously highlighted by genome-wide association (GWAS SNPs) are displayed as black triangles.

# DISEASE RESISTANCE: GENERAL IDEA

THREE GENERAL APPROACHES:

1. CANDIDATE GENES
2. GENOME-WIDE ASSOCIATION STUDIES
3. TRANSCRIPTOMICS

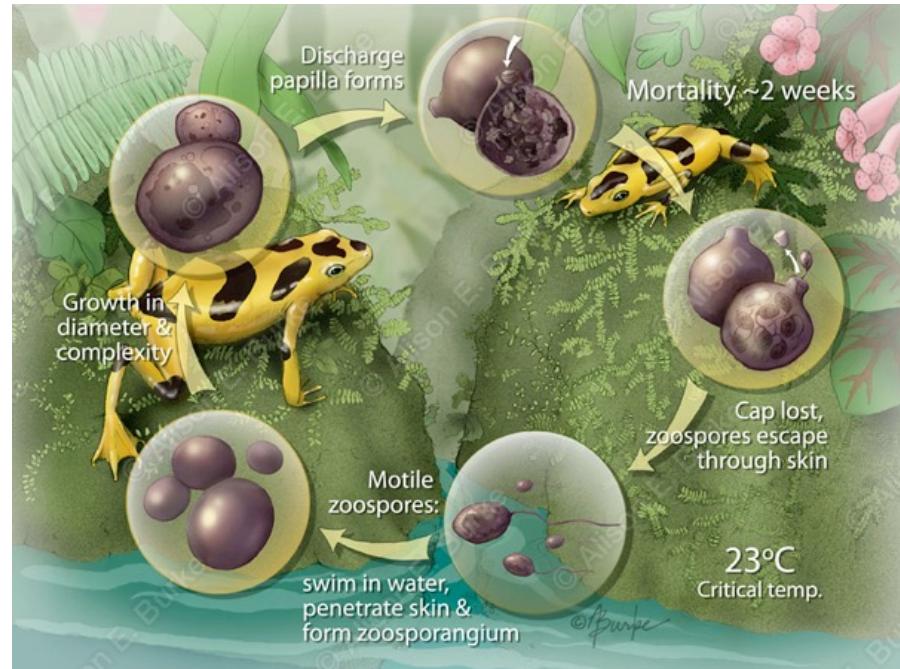
# DISEASE RESISTANCE: CANDIDATE GENE EXAMPLE



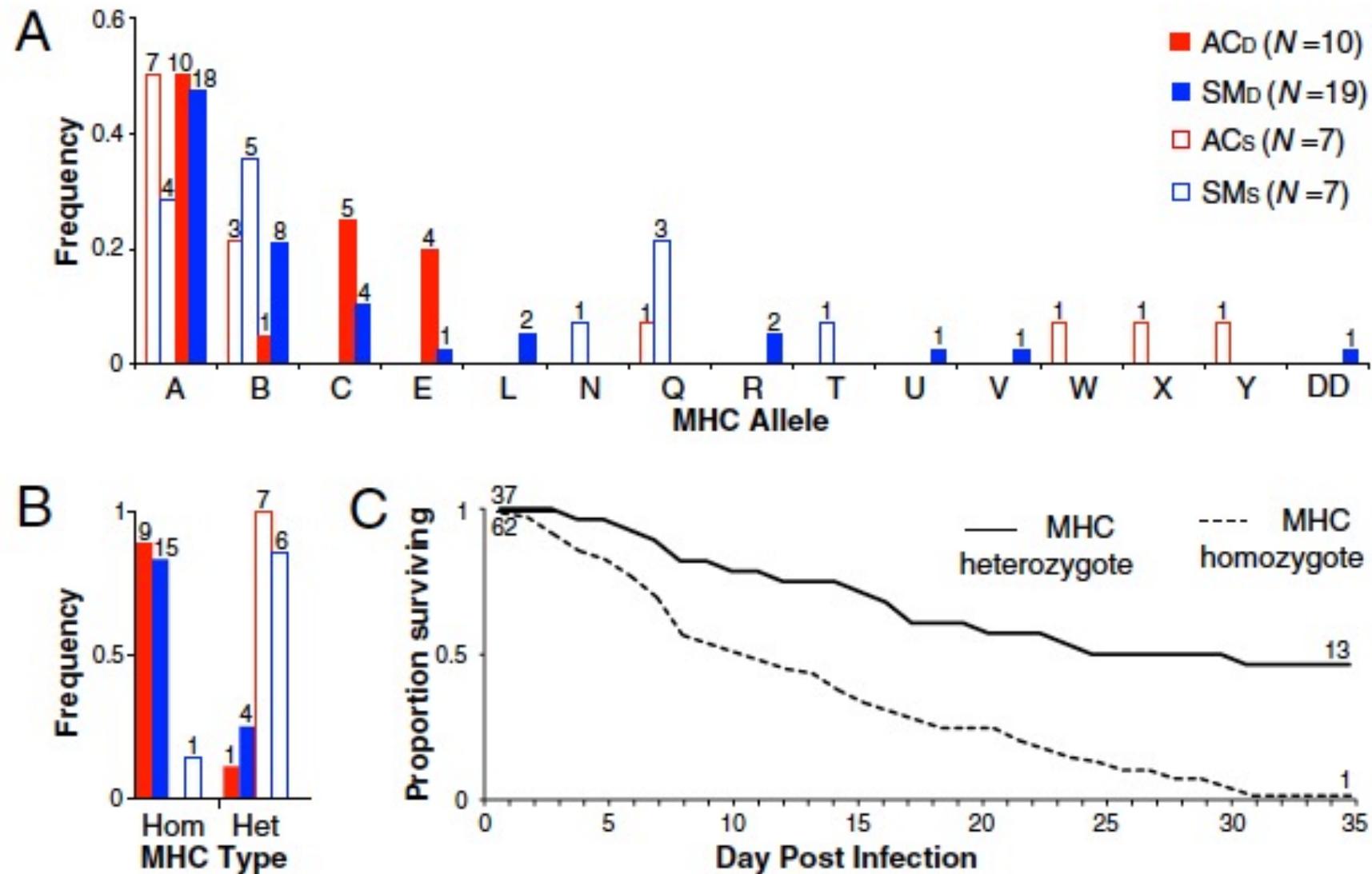
## MHC genotypes associate with resistance to a frog-killing fungus

Anna E. Savage<sup>1</sup> and Kelly R. Zamudio

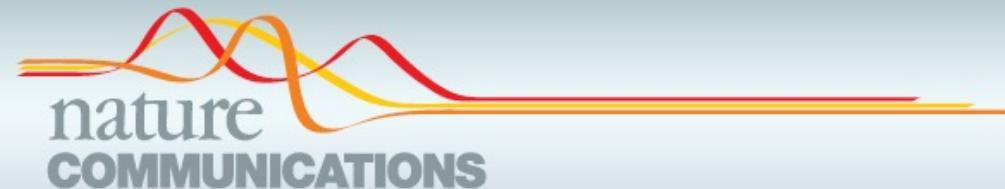
Department of Ecology and Evolutionary Biology, Cornell University, Ithaca, NY 14853



# DISEASE RESISTANCE: CANDIDATE GENE EXAMPLE



# DISEASE RESISTANCE: GWAS EXAMPLE



## ARTICLE

Received 31 Mar 2016 | Accepted 20 Jul 2016 | Published 30 Aug 2016

DOI: 10.1038/ncomms12684

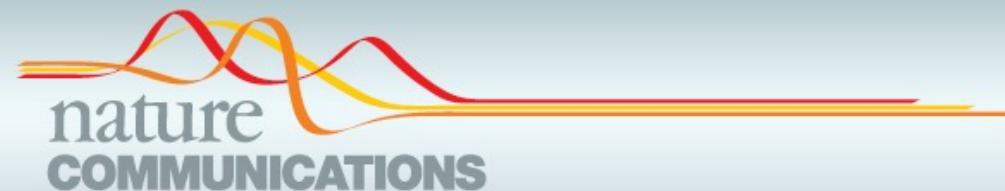
OPEN

## Rapid evolutionary response to a transmissible cancer in Tasmanian devils

Brendan Epstein<sup>1</sup>, Menna Jones<sup>2</sup>, Rodrigo Hamede<sup>2</sup>, Sarah Hendricks<sup>3</sup>, Hamish McCallum<sup>4</sup>, Elizabeth P. Murchison<sup>5</sup>, Barbara Schönfeld<sup>2</sup>, Cody Wiench<sup>3</sup>, Paul Hohenlohe<sup>3,\*</sup> & Andrew Storfer<sup>1,\*</sup>



# DISEASE RESISTANCE: GWAS EXAMPLE



## ARTICLE

Received 31 Mar 2016 | Accepted 20 Jul 2016 | Published 30 Aug 2016

DOI: 10.1038/ncomms12684

OPEN

## Rapid evolutionary response to a transmissible cancer in Tasmanian devils

Brendan Epstein<sup>1</sup>, Menna Jones<sup>2</sup>, Rodrigo Hamede<sup>2</sup>, Sarah Hendricks<sup>3</sup>, Hamish McCallum<sup>4</sup>, Elizabeth P. Murchison<sup>5</sup>, Barbara Schönfeld<sup>2</sup>, Cody Wiench<sup>3</sup>, Paul Hohenlohe<sup>3,\*</sup> & Andrew Storfer<sup>1,\*</sup>



# DISEASE RESISTANCE: TRANSCRIPTOMICS EXAMPLE

## MOLECULAR ECOLOGY

Molecular Ecology (2016) 25, 5663–5679

doi: 10.1111/mec.13871

### Comparative study of host response to chytridiomycosis in a susceptible and a resistant toad species

T. J. POORTEN and E. B. ROSENBLUM

*Department of Environmental Science, Policy and Management, University of California, Rm. 54 Mulford Hall, Berkeley, CA, USA*



# DISEASE RESISTANCE: TRANSCRIPTOMICS EXAMPLE

**Table 1** Summary of gene expression results from GO stats enrichment analysis

Group		No. of DE probesets*	No. of enriched GO Terms <sup>†</sup>	Selected enriched GO Terms
Skin: Upregulated				
	<i>Bufo marinus</i>	487	66	Epidermis development; wound healing; cell proliferation; apoptotic signalling pathway; response to stress; metabolic process; biological adhesion; immune system development
	<i>Bufo boreas</i>	1108	68	Regulation of complement activation; response to stress; wound healing; cell redox homeostasis; response to external stimulus; response to yeast; haematopoietic or lymphoid organ development; leucocyte migration; apoptotic process; cellular metabolic process; innate immune response; coagulation
Skin: Downregulated				
	<i>B. marinus</i>	70	2	Cellular localization; metabolic process
	<i>B. boreas</i>	1055	58	Collagen catabolic process; extracellular structure organization; blood vessel development; response to wounding; haemostasis; cell-matrix adhesion; tissue development; epithelium development; actin cytoskeleton organization
Liver: Upregulated				
	<i>B. marinus</i>	0	NA	—
	<i>B. boreas</i>	1947	70	Vesicle-mediated transport; protein folding; regulation of cell cycle; cellular metabolic process; RNA processing; cellular respiration; cell proliferation; response to stress
Liver: Downregulated				
	<i>B. marinus</i>	2	NA	—
	<i>B. boreas</i>	951	74	Actin filament organization; wound healing; response to stress; immune system process; complement activation; antigen processing and presentation of peptide antigen; innate immune response; blood coagulation; blood vessel morphogenesis
Spleen: Upregulated				
	<i>B. marinus</i>	0	NA	—
	<i>B. boreas</i>	0	NA	—
Spleen: Downregulated				
	<i>B. marinus</i>	0	NA	—
	<i>B. boreas</i>	3	NA	—

\*Differential expression (DE) threshold criteria for *B. marinus* was BH-corrected *P*-value < 0.1; and for *B. boreas* was BH-corrected *P*-value < 0.05.

<sup>†</sup>List of 'Biological Process' category GO terms was reduced using Revigo to remove semantic redundancies.

# DISEASE RESISTANCE: INBREEDING DEPRESSION-DISEASE INTERACTION EXAMPLE

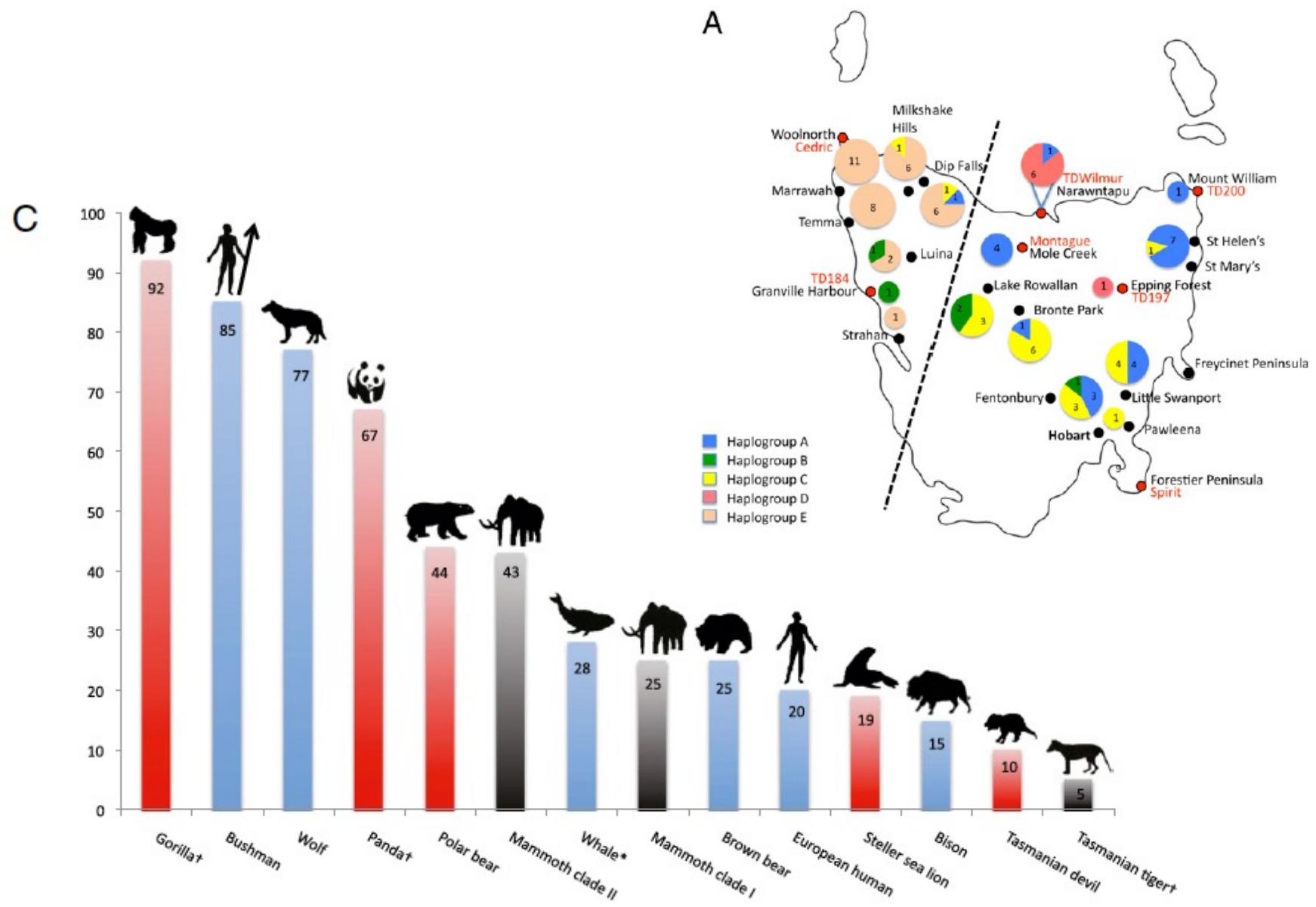
PNAS

## Genetic diversity and population structure of the endangered marsupial *Sarcophilus harrisii* (Tasmanian devil)

Webb Miller<sup>a,1</sup>, Vanessa M. Hayes<sup>b,c,1,2</sup>, Aakrosh Ratan<sup>a</sup>, Desiree C. Petersen<sup>b,c</sup>, Nicola E. Wittekindt<sup>a</sup>, Jason Miller<sup>c</sup>, Brian Walenz<sup>c</sup>, James Knight<sup>d</sup>, Ji Qi<sup>a</sup>, Fangqing Zhao<sup>a</sup>, Qingyu Wang<sup>a</sup>, Oscar C. Bedoya-Reina<sup>a</sup>, Neerja Katiyar<sup>a</sup>, Lynn P. Tomsho<sup>a</sup>, Lindsay McClellan Kasson<sup>a</sup>, Rae-Anne Hardie<sup>b</sup>, Paula Woodbridge<sup>b</sup>, Elizabeth A. Tindall<sup>b</sup>, Mads Frost Bertelsen<sup>e</sup>, Dale Dixon<sup>f</sup>, Stephen Pyecroft<sup>g</sup>, Kristofer M. Helgen<sup>h</sup>, Arthur M. Lesk<sup>a</sup>, Thomas H. Pringle<sup>i</sup>, Nick Patterson<sup>j</sup>, Yu Zhang<sup>a</sup>, Alexandre Kreiss<sup>k</sup>, Gregory M. Woods<sup>k,l</sup>, Menna E. Jones<sup>k</sup>, and Stephan C. Schuster<sup>a,1,2</sup>



# DISEASE RESISTANCE: INBREEDING DEPRESSION-DISEASE INTERACTION EXAMPLE



# PAIRS: “FLASH” HOST POP GENOMICS RESEARCH DESIGN

## INSTRUCTIONS:

1. COME UP WITH QUESTION & HYPOTHESIS FOR YOUR HOST SPECIES RELATED TO DISEASE
1. DISCUSS WHICH GENOMIC APPROACHE(S) WOULD BEST TEST YOUR HYPOTHESIS
2. IN ~10 MINS, WILL DISCUSS RESEARCH IDEAS WITH GROUP

