

Outline – Introduction to FAANG Consortium

1. Why FAANG?
2. FAANG history, goals, and activities
3. Current USDA FAANG projects
4. FAANG data available → getting involved

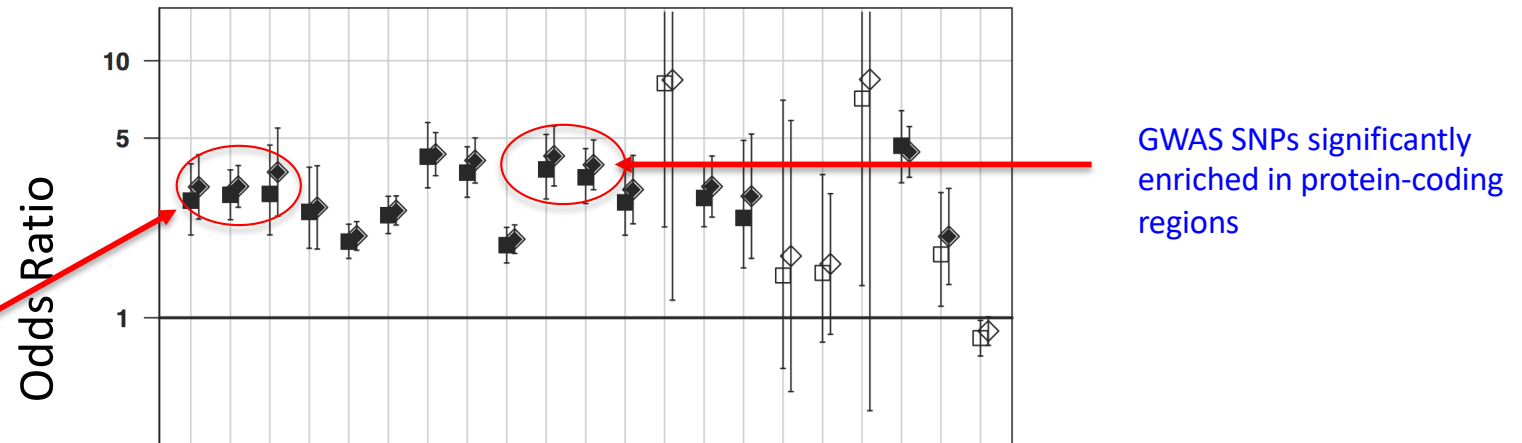
Why is FAANG important?

- Understanding the genotype to phenotype link:
 - Improving fundamental understanding of biology
 - Providing information to accelerate genetic improvement- *linking trait-associated SNP with function at that SNP location*
- Thus we need to *annotate the function* of the genome of our animals

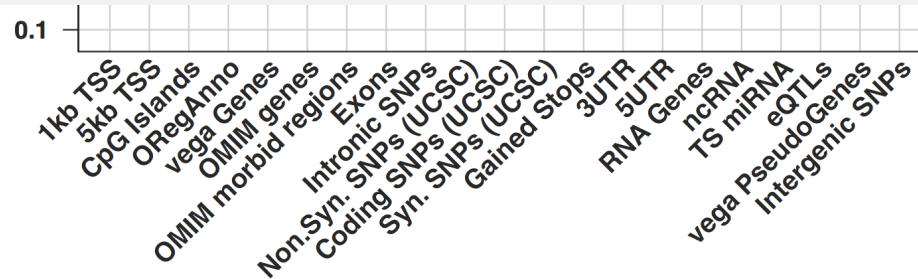
Why is functional annotation important?

Is trait-associated genetic variation located (enriched) in genes?

Yes!



But also enriched in regions flanking/outside known coding regions!



- Permutations
- ◇ Random Sampling
- | 95% CI
- Significant Odds Ratios



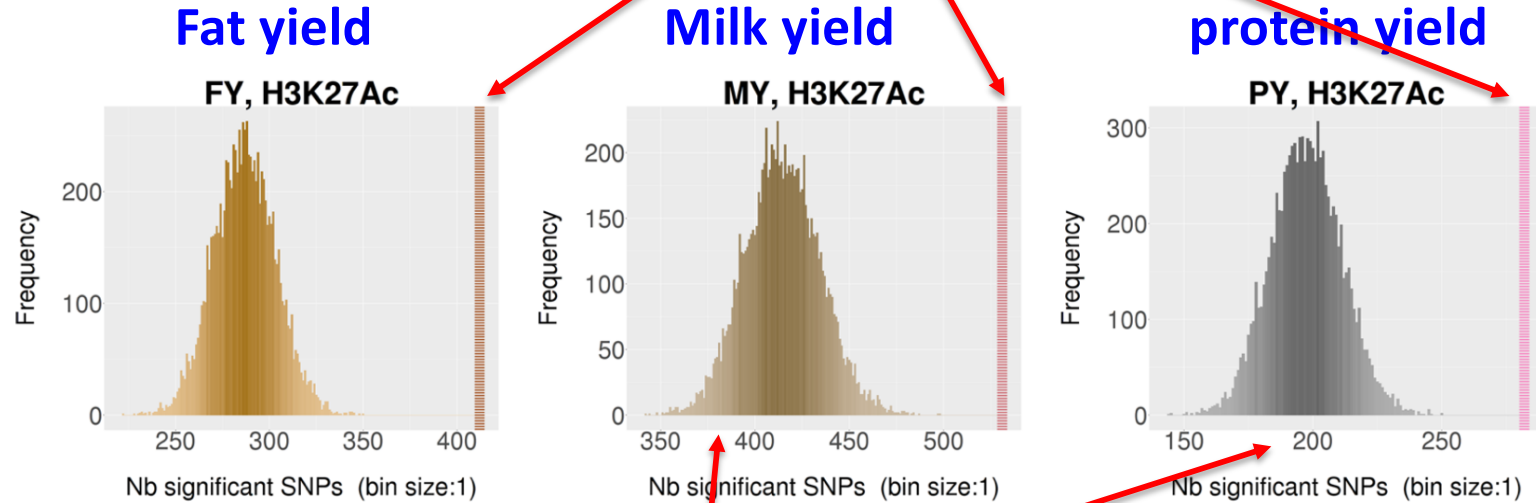
The genomic signature of trait-associated variants

Alida S D Kindt, Pau Navarro, Colin A M Semple and Chris S Haley*

BMC Genomics 2013 14:108

Shown in livestock as well: Milk trait-associated SNPs enriched in predicted regulatory regions

Many sig SNPs in bovine enhancer regions predicted from mapping ENCODE to bovine genome



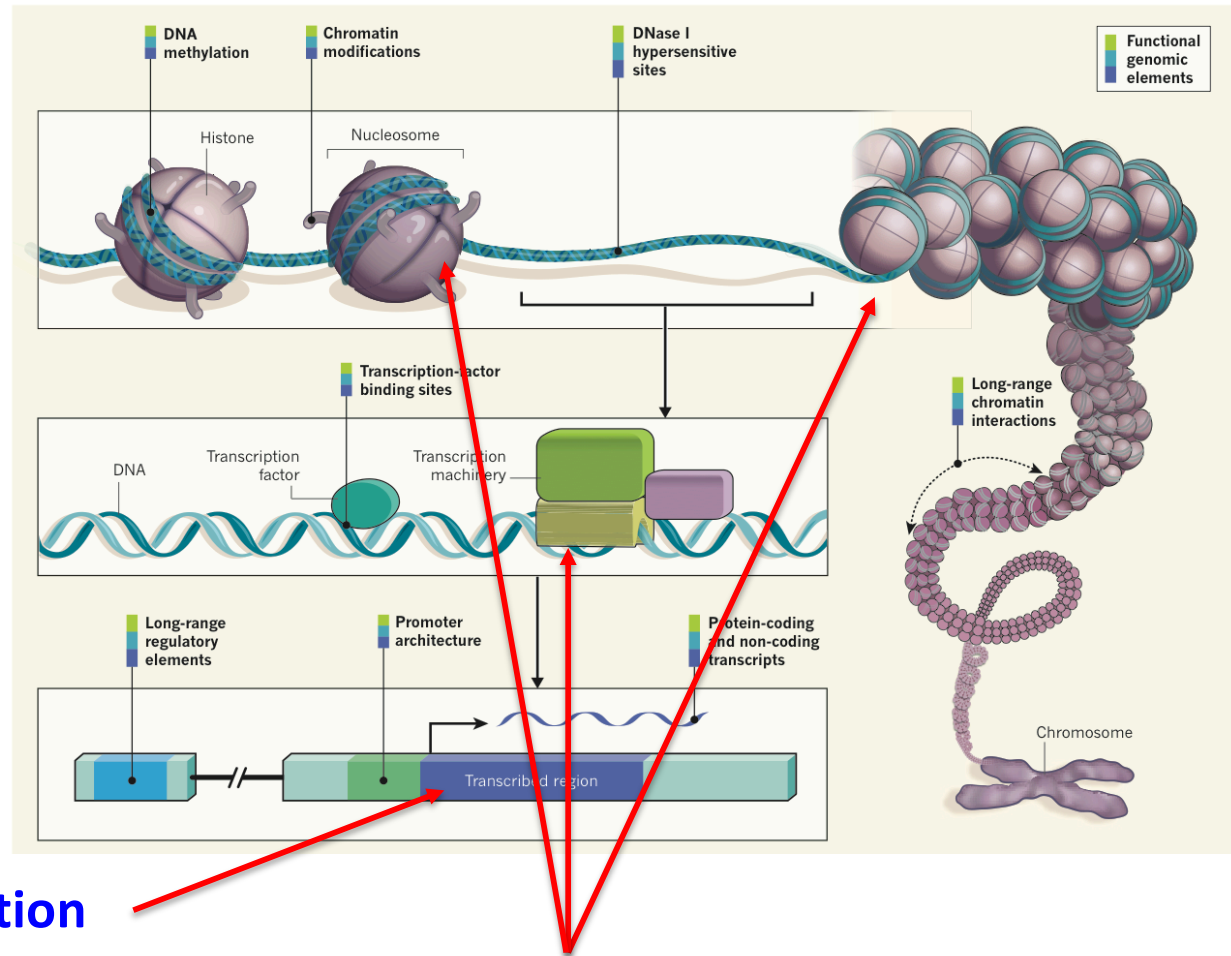
Much fewer sig SNPs in random sampling

Large-scale genome functional annotation: *described by ENCODE*

To understand function:

a) what part is expressed?

b) what part controls this expression (specific tissue or cell type, response to infection, etc):



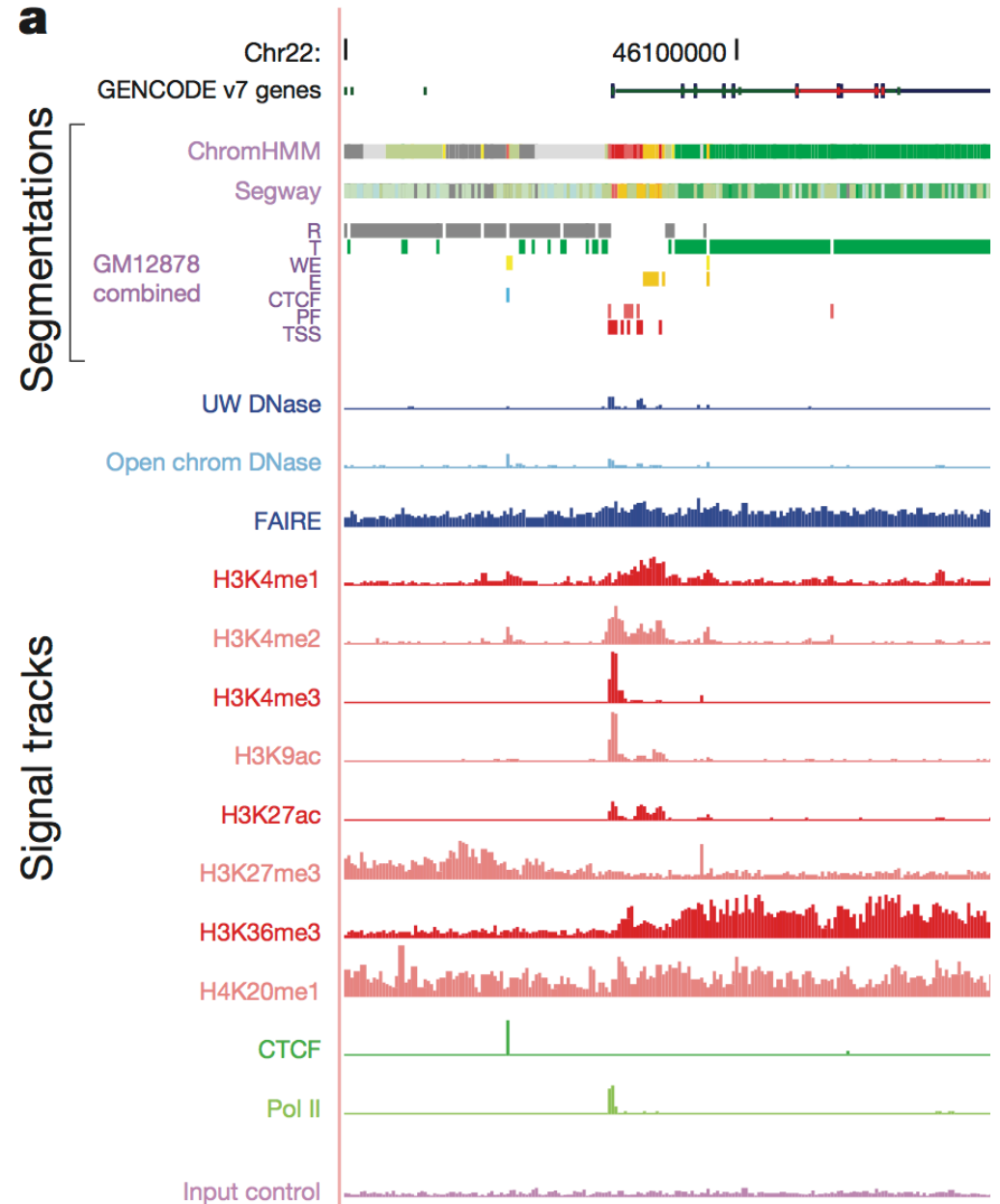
RNA levels and location

Biochemical assays of Chromatin structure

Functional Annotation results

Collecting all these data on the same samples allowed *predictive models for genome function* to be developed for each part of genome

- Predicts Chromatin State: OPEN or CLOSED
- Created a functional map of genome segments



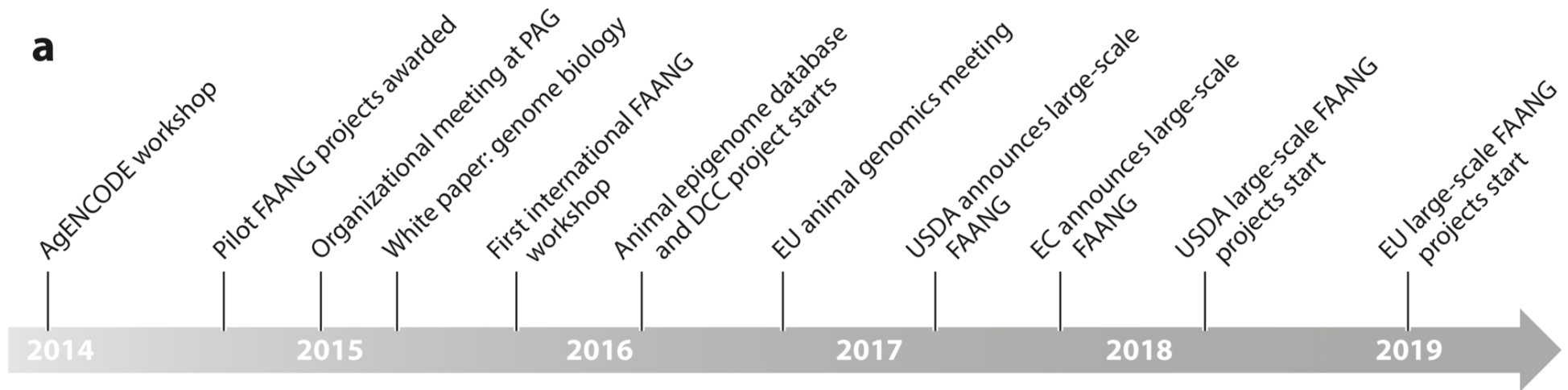
Success in ENCODE required:

- High quality reference genome sequence
- Common infrastructure providing
 - Biological resources
 - Bioinformatics tools
 - Databases
- Effective coordination and communication

FAANG needs all these to succeed!

Brief FAANG history

- Workshop in January 2014
- Organizational meeting in Jan 2015 in San Diego
- White paper published in 2015-- “Highly accessed”
 - > 9,400 accesses as of March 2019, 82 citations
- 2015 1st International Workshop + 2016 EU AG meetings to kick off FAANG
→ inter-agency discussions for increased funding
- 2018, 2019 large resource projects started



Giuffra, Tuggle, et al.,
*Annual Reviews in Animal
Biosciences February 2019*

Functional Annotation of Animal Genomes (FAANG): Current Achievements and Roadmap

Annual Review of Animal Biosciences

Vol. 7:65-88 (Volume publication date February 2019)

First published as a Review in Advance on November 14, 2018

<https://doi.org/10.1146/annurev-animal-020518-114913>

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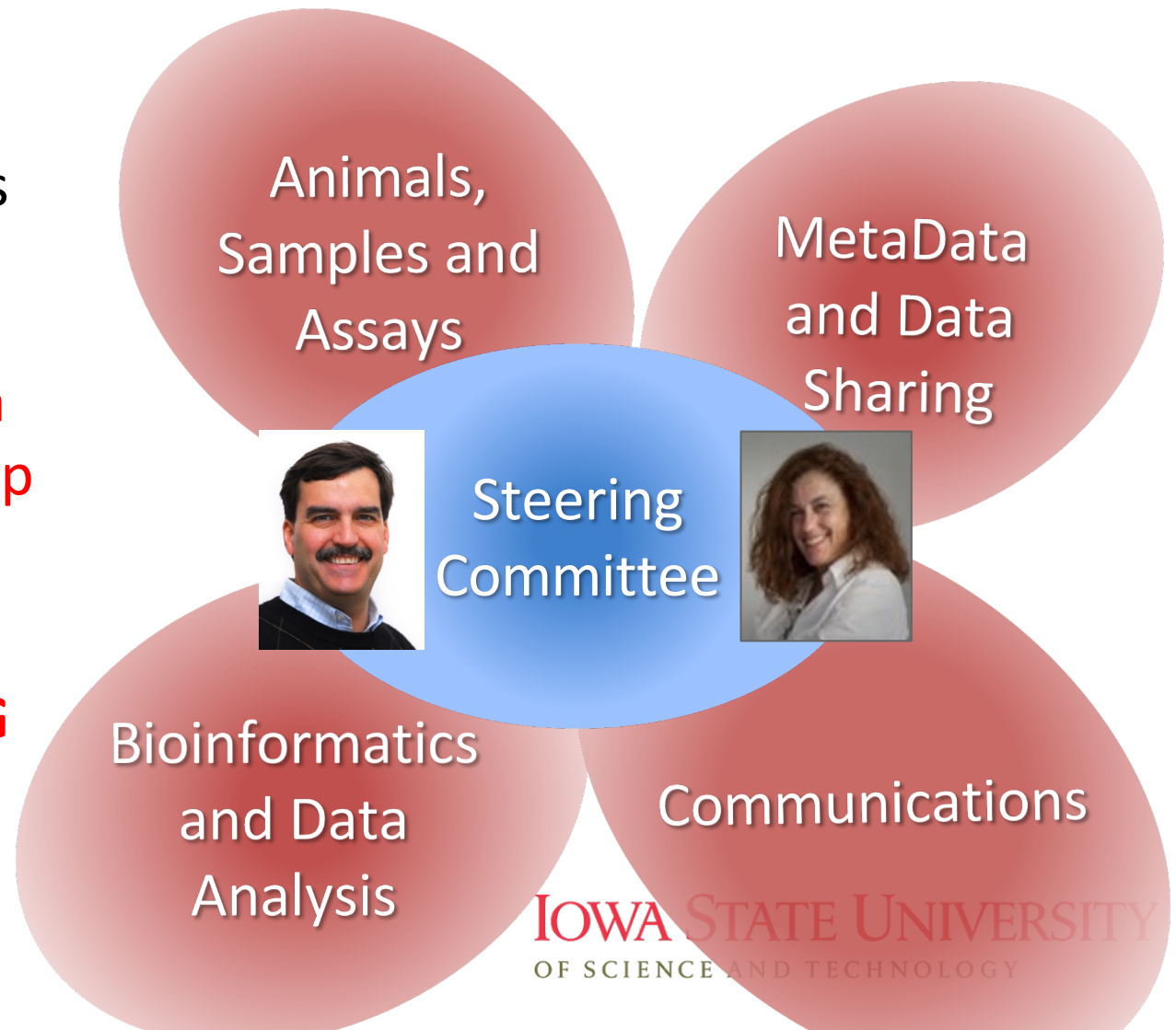
FAANG: Current activities

FAANG globally coordinates functional annotation across species for efficiency, comparisons

FAANG Committees have conference calls on-line periodically

FAANG members can self-select membership in these committees

Anyone can participate in FAANG activities!



Main current activities

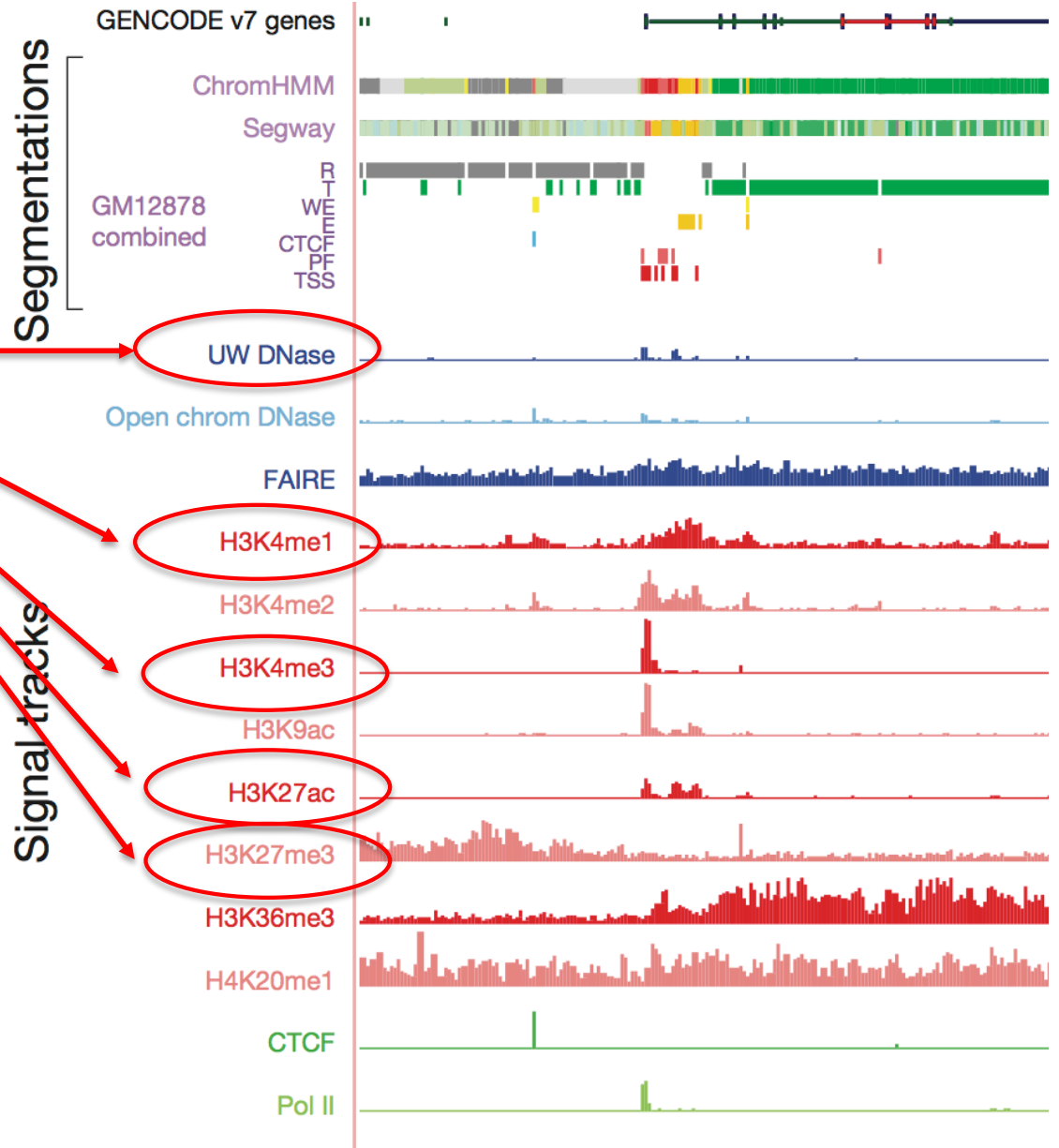
- **Phase I**
 - Emphasis on establishing reference datasets for healthy adults
 - Few biological replicates, no treatments
 - Validate metadata toolboxes and analytical pipelines
- **Phase II**
 - Expand biological states- treatments, developmental stage, genetic variation

Core assays needed for chromatin state modeling

- **RNAseq (stranded, deep) analysis of many tissues from the same 2-4 individuals**
- **Chromatin accessibility/architecture assays on these tissues (DNase I or ATAC-seq)**
- **Histone modification marks**
 - **H3K4 monomethylation**
 - **H3K4 trimethylation**
 - **H3K27acetylation**
 - **H3K27 trimethylation**

Minimum information for finding functional regions in livestock genomes

FAANG core assays



Core assays needed for modeling

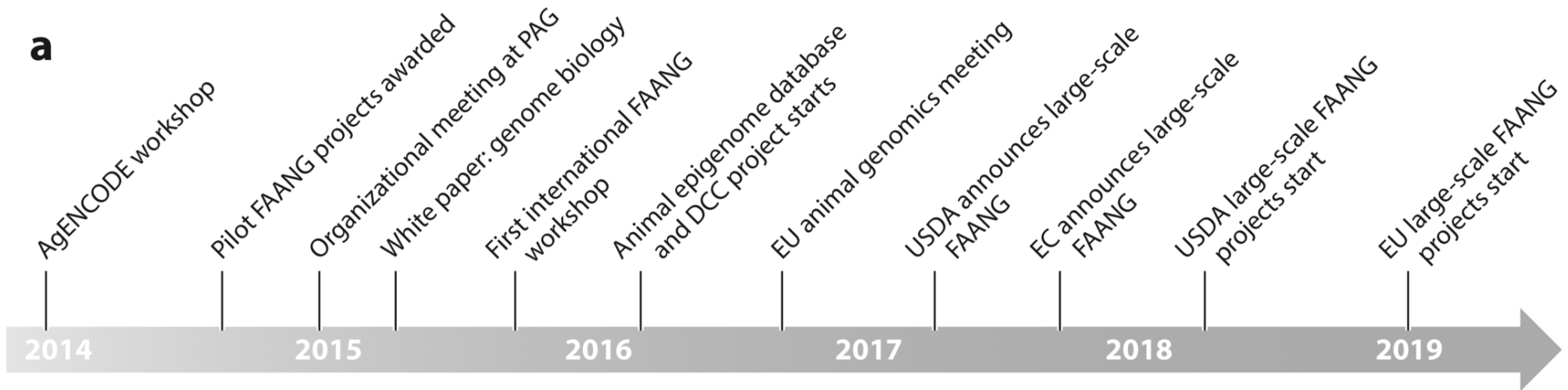
- RNAseq (stranded, deep) analysis of as many tissues from the same 2-4 individuals
- Chromatin accessibility/architecture assays on these tissues (DNase I or ATAC-seq)
- Histone modification marks
 - H3K4 monomethylation
 - H3K4 trimethylation
 - H3K27acetylation
 - H3K27 trimethylation

Additional assays to determine genome function

- **DNA methylation**
- **Regulatory factor protein binding (CTCF)**
- **Chromatin interaction (Hi-C)**

Brief FAANG history

- Multi-species, Phase 1 pilot projects in US and France
- USDA large-scale projects started in 2018
- EU large-scale projects started in 2019



Giuffra, Tuggle, et al., *Annual Reviews in Animal Biosciences*
February 2019

FAANG projects- an early list

Species	Leading Inst. & country	<i>FAANG- FAANG-</i>	
		<i>pilot</i>	<i>rel.</i>
pig, cattle, goat, chicken	INRA France	X	x
pig, cattle, chicken	UC-Davis US	X	x
horse	UC-Davis & Nebraska Univ. US	X	x
cattle	Leibniz Inst. for Farm Anim. Biology Germany	X	x
Sheep	Int. Sheep Genome Consortium & others Australia & US	X	x
pig, chicken	Wageningen Univ. The Netherlands	X	X
cattle	Dairy Futures Coop. Res. Centre, AgriBio & others Australia	X	X
cattle, pig	Alberta & Guelph Univ. & others Canada	x	X
cattle and zebu	Adelaide Univ. Australia	x	X
sheep, buffalo	Roslin- Edinburgh Univ. UK	x	X
cattle	Washington State Univ. US	x	X
'Arctic Ark'	Natural Resources Institute Finland		X

Progress on UCD FAANG Pilot project H. Zhou et al.



United States Department of Agriculture
National Institute of Food and Agriculture



RNA-seq	Submitted	Submitted	Submitted
DNase/ATAC-seq	Submitted	Data Analysis	Data Analysis
H3K4me3	Data Analysis	Data Analysis	Data Analysis
H3K27me3	Data Analysis	Data Analysis	Data Analysis
H3K4me1	Data Analysis	Data Analysis	Data Analysis
H3K27ac	Data Analysis	Data Analysis	Data Analysis
CTCF	Data Analysis	Data Analysis	Data Analysis
RRBS-seq	Submitted	Submitted	Data Analysis

Spleen tissue submitted

Remaining data will be submitted in the coming weeks

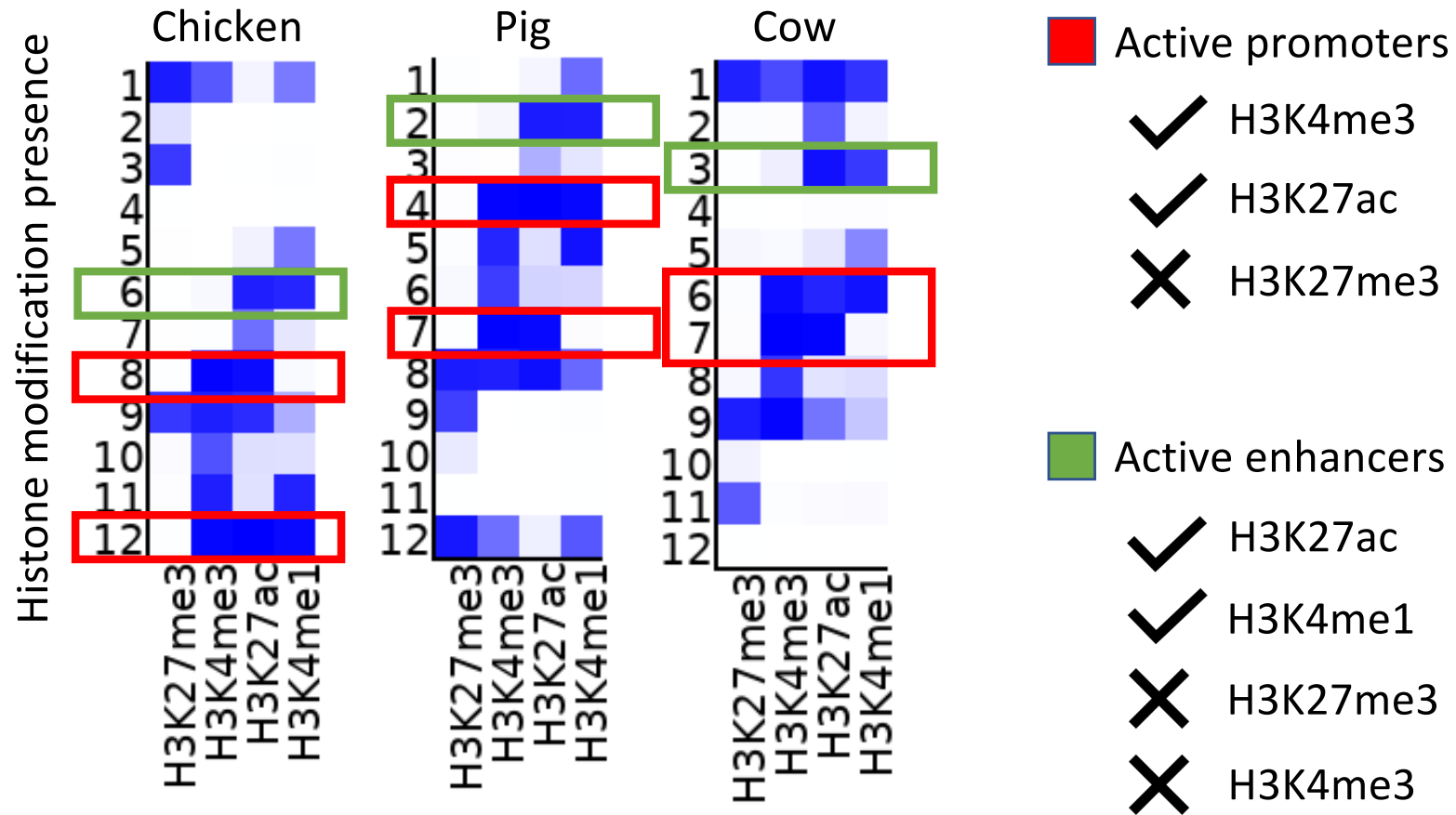
Poultry, Cattle,
Swine Genome
Coordination
Funds

Data available at <http://data.faang.org/dataset/PRJEB14330>



IOWA STATE UNIVERSITY
OF SCIENCE AND TECHNOLOGY

UCD FAANG Pilot: Chromatin state models across 8 tissues



UCD FAANG Pilot presentations at ISAG 2019

Presentations:

Monday: Epigenetics – Tues/Thurs poster

OP05/P014 M. Halstead. Identification of orthologous tissue-specific enhancer-gene pairs across chicken, pig and cattle

OP12 C. Kern. Allele-specific chromatin accessibility and histone modifications in an F1 cross of MD resistant and susceptible chicken lines

Monday: Genetics of Immune Response and Disease Resistance Mon/Wed poster

OP28/P009 G. Chanthavixay. Differential H3K27ac peaks within bursa tissue of two inbred chicken lines under NDV infection and heat stress

Future of livestock functional genomics

- **Three new projects started in 2018, funded by new USDA-NIFA-AFRI funding to the Animal Genome program**
 - ***Cattle***
 - ***Chicken***
 - ***Pig***
- ***Major goals- add substantial data to existing functional data in these three species***

Genome wide annotation of cis-regulatory elements in the chicken genome

USDA-NIFA

Yvonne Drechsler, PhD (Western University of Health Sciences)

David R. Hawkins, PhD (University of Washington)



Years 1-2 (\$1M in initial funding)

- Cells and Tissues targeted:
 - Peripheral blood monocytes/macrophages
 - Peripheral blood B-cells
 - Peripheral blood CD4 T cells, polarized to Th1 and Th2
 - Lung macrophages
 - Female reproductive tract: Ovaries, Oviduct split into Isthmus, Magnum and Shell gland

Progress in Year 1

Ovary, Oviduct sections, monocytes and B-cells:

RNA and ATAC seq are in data analysis

WGBS Libraries passed initial QC, queued for full sequencing

ChIP-seq libraries generated for five histone modifications:

H3K4me3, H3K4me1, H3K27ac, H3K27me3, and H3K36me3.

Sequencing and QC analysis are currently underway.

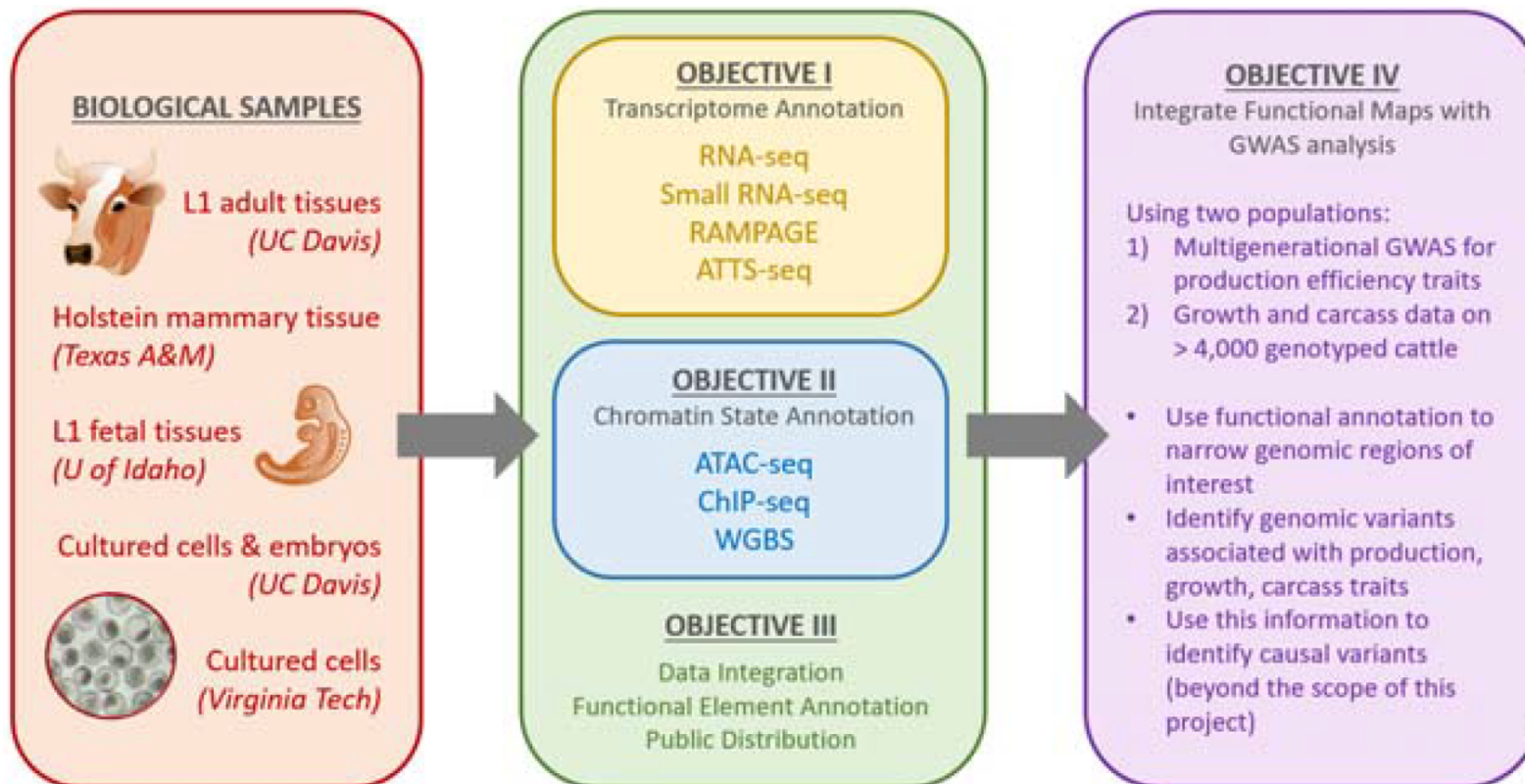
T cells: in progress

Functional Annotation of the Bovine Genome

USDA-NIFA-AFRI GRANT NO: 2018-67015-27500

Pablo Ross, Stephanie McKay, Monique Rijnkels, Brenda Murdoch, Tim Smith, Clare Gill, Huaijun Zhou, Zihua Jiang, James Reecy, Wansheng Liu, Honglin Jiang, Milton Thomas

University of California Davis, University of Vermont, Texas A&M University, University of Idaho, USDA-ARS, Washington State University, Iowa State University, Pennsylvania State University, Virginia Tech, Colorado State University



Functional Annotation of the Bovine Genome

Ross PJ (UCD), McKay S (UV), Rijnkels M (TAMU), Murdoch B (UI), Smith T (USDA-ARS), Gill C (TAMU), Zhou H (UCD), Jiang Z (WSU), Reecy J (ISU), Liu W (PSU), Jiang H (VT), Thomas M (CSU) USDA-NIFA-AFRI 2018-67015-27500

- 40 adult tissues from L1 Hereford line
- 8 fetal tissues from L1 Hereford line
- 8 primary cell lines
- 5 stages of Holstein mammary gland development



ASSAYS-BY-SEQUENCE

Expressed regions

RNA-seq	Large transcripts expression - variants
smRNA-seq	Small transcript expression
RAMPAGE	Transcription start sites - Expression levels
WTTS-seq	Transcription termination sites
Iso-seq	Transcript variant discovery

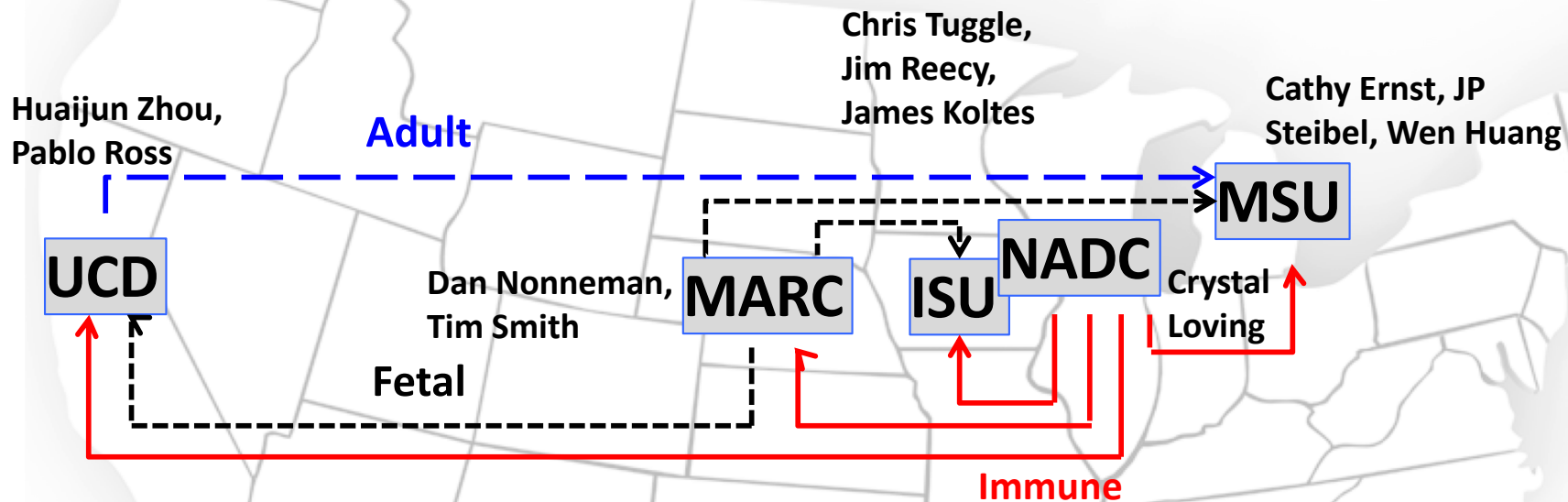
Chromatin states

	WGBS	DNA methylation
	ATAC-seq	Open Chromatin profiling
CHIP-seq	H3K4me3	Active promoters
	H3K27me3	Polycomb repression
	H3K4me1	Active enhancers
	H3K27ac	Enhancers and promoters
	CTCF	Insulators and promoters
	H3K9me3	Heterochromatin
	H3K36me3	Active gene bodies

Functional Annotation of the Porcine Genome

- ***Overall goal: catalog functional elements in the porcine genome for many biological states, create Chromatin state map***
- **Aim 1 Adult tissues**
 - extend FAANG pilot of 8 -> 25 tissues
- **Aim 2 Fetal tissues**
 - Correlate allele-specific expression and chromatin modification
 - Parent-of-origin effects (reciprocal crosses Meishan x WhiteCross)
- **Aim 3 Immune System**
 - Circulating Blood Cells- flow-sorted into functional types
 - *Single cell analysis of blood PMBC and immune tissues*
- **Aim 4 Data Integration**
 - Integrate all public and project data to develop a higher-order regulatory understanding of the porcine genome, including a predicted chromatin state map.

Pig FAANG: Community Sharing of Samples and Expertise



Location	Tissue collection	Sample Analyses
ISU	None	Histone CHIP, ATAC-Seq
MARC	Fetal*	RNAseq, IsoSeq
MSU	None#	DNA Methylation (WG-BS)
NADC	Immune	None
UCD	Adult#	Histone CHIP, ATAC-Seq, RAMPAGE

*Fetal Tissue already collected

Some adult tissues to be collected at MSU through 2016 AFRI project to UCD

DELIVERABLES

1. Novel porcine **transcriptomic and epigenetic information on the genes and regulators** controlling expression in **~40 biological states** (~18 adult, four fetal tissues at two stages of development, eight blood cell types during healthy growth and macrophages during responses to two models of infection at two times post-stimulation).
2. **Prediction of the function of genomic regions** across tissues and cells relevant for prioritizing SNPs associated with specific phenotypes related to these tissues/cells

Getting Involved: Resources

- FAANG website www.faang.org
- FAANG Publications
- FAANG meetings (talk ppts available)



Member home | About FAANG | Projects & Fundings | Publications | Meetings

FAANG
Functional Annotation of Animal Genomes

Functional Annotation of ANimal Genomes (FAANG) Project
— A coordinated international action to accelerate Genome to Phenome

Publications

Landmark Papers:

Review
Elisabetta Giuffra, Christopher K. Tuggle and The FAANG Consortium (2019), **Genomes (FAANG): Current Achievements and Roadmap**. *Annual Review of Animal Biosciences*, Vol. 7

GO-FAANG
Tuggle, C. K., Giuffra, E., White, S. N., Clarke, L., Zhou, H., Ross, P. J., Acloque, H., Reecy, J. M., Archibald, A., Bellone, R. R., Boichard, M., Chamberlain, A., Cheng, H., Crooijmans, R. P.M.A., Delany, M. E., Finno, C. J., Groenen, M. A. M., Hayes, B., Lunney, J. K., Petersen, J. L., Plastow, G. S., Schmidt, C. J., Song, J. and Watson, M. (2016), **GO-FAANG meeting: a Gathering On Functional Annotation of Animal Genomes**. *Anim Genet*, 47: 528-533

WhitePaper
The FAANG Consortium (2015), "Coordinated international action to accelerate Genome to Phenome, The Functional Annotation of ANimal Genomes (FAANG) Project". *Genome Biology* 2015, 16:57.

A coordinated

FAANG Aims:

- Standardize core ass
- Coordinate and facilit
- Establish an infrastru
- Provide high quality f genomes

Sign up here t



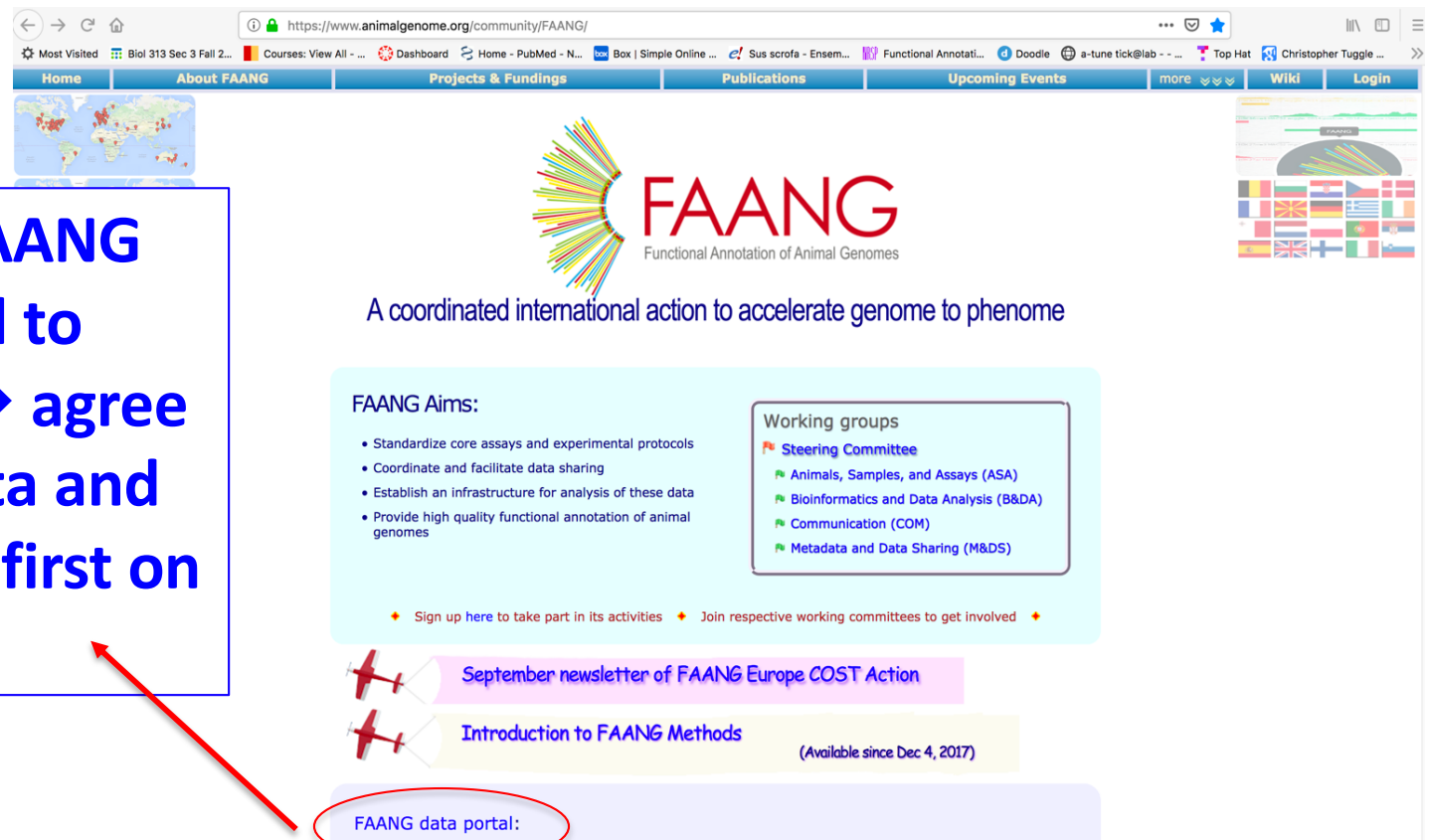
FAANG data port

Archives from previous meetings

- FAANG at PAG-XXVII (PAG 2019)
Dates: Jan. 11, 2019
Location: Town & Country, San Diego, CA
Archives: Power point slides, PDF, etc.
Status: Held as planned
- 7th International Symposium on Animal Functional Genomics & Functional Annotation of Animal Genomes Workshop 2018
Dates: Nov. 12-15, 2018
Location: Adelaide, Australia
Archives: Proceedings (PDF)
Status: Held as planned
- FAANG at PAG-XXVI (PAG 2018)
Dates: Jan. 12, 2018
Location: Town & Country, San Diego, CA
Archives: Power point slides, PDF, etc.
Status: Held as planned

Getting Involved: Resources

- FAANG data portal: <http://data.faang.org>
- Data Coordination Centre --> *in details by Elisabetta Giuffra*



The screenshot shows the FAANG website homepage. At the top, there is a navigation bar with links for Home, About FAANG, Projects & Fundings, Publications, Upcoming Events, Wiki, and Login. Below the navigation bar is a world map and the FAANG logo, which consists of a stylized sunburst of colorful lines. The main heading reads "FAANG Functional Annotation of Animal Genomes". Below this, a tagline states "A coordinated international action to accelerate genome to phenome". The page is divided into several sections: "FAANG Aims:" with a list of four bullet points; "Working groups" with a list of four groups: Steering Committee, Animals, Samples, and Assays (ASA), Bioinformatics and Data Analysis (B&DA), Communication (COM), and Metadata and Data Sharing (M&DS); and a section for "September newsletter of FAANG Europe COST Action" and "Introduction to FAANG Methods (Available since Dec 4, 2017)". At the bottom, there is a blue button labeled "FAANG data portal:" which is circled in red. A red arrow points from this button to a text box on the left.

Access to FAANG data limited to members → agree to share data and not publish first on others data

