Building the Tools to Solve the Genome to Phenome Puzzle in Agriculture

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USDA-NIFA Agricultural Genome to Phenome Initiative

- 2018 Farm Bill directed NIFA to establish a new competitive grant program to support research concerning genomes and phenomes of crops and animals of importance to US agriculture, authorizing up to ***$40,000,000 annually 2019 - 2023***.

  - https://nifa.usda.gov/program/genome-phenome-initiative

- U.S. Congress appropriated <u>only</u> ***$1M in fiscal year 2020***

  $1M in fiscal year 2021

  $2M in fiscal year 2022

What's Required to Realize this Vision?

- A **community** of interactive biologists (crop + livestock), engineers, data scientists and members of the greater community

- More **data** (phenotypes, genotypes and environment/management practices) ideally from coordinated, multi-disciplinary, multi-location, multi-year projects

> Genotype (G) + Environment (E) + G x E = Phenotype (P)

- New **technologies** and analysis methods

- Substantial new **R&D investments**

External Stakeholder Member Organizations

AG2PI — Agricultural Genome to Phenome Initiative

Role of Stakeholder Organizations

- Link communication between AG2PI, organization employees and members, including sharing AG2PI news and events
- Participate in AG2PI activities, including contributing materials or expertise
- Provide feedback through surveys and one-on-one communication with AG2PI executive board members

Poultry Breeders of America

Activities & Deliverables 2020 grant ($1M)

AG2PI — Agricultural Genome to Phenome Initiative

Field Days

Training Workshops

Community Surveys

Conferences

Seed Grants

Seed Grants RFP
Training Workshops
Conferences
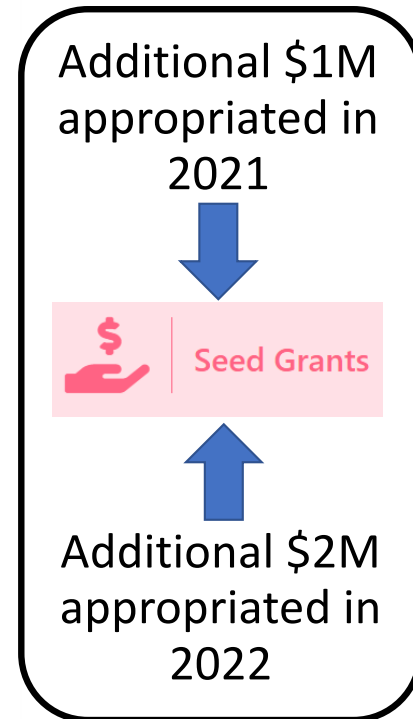Field Days

Advisory Group Meetings

Deliverables

Year 2

Inform

White Paper

Advisory Group Contact

Year 1

Community Survey

Inform

Seed Grants
Training Workshops
Conferences
Field Days

White Papers, Steering Committee, and Advisory Groups

Inform

Advisory Group Meetings

Deliverables

Inform

Year 3

Final White Paper(s) and Recommendations

Inform

Seed Grants Reports
Training Workshops
Conferences
Field Days

Deliverables

Advisory Group Meetings

Additional $1M appropriated in 2021

Seed Grants

Additional $2M appropriated in 2022

Project Summary | People | Institutional Involvement | Get Involved | Workshops & Activities 2 | Seed Grants RFP 3 | Publications | Community Surveys | Community Events | Resources | Contact Us

Goals

- Expose Ag G2P community to research activities and resources across crops and livestock
- Share research methods, approaches, capacities
- Identify research and capacity gaps and challenges for AG2P research
- Provide a platform for introducing teams that can develop joint solutions

Selection of Past Field Day Topics:
- Automating Phenotyping
- Genomic Selection and Phenotyping in Dairy Cattle
- U.S. Aquaculture
- Precision Livestock Management
- Breeding Challenges in Fruit Trees
- AI and Agriculture
- IP in Livestock and Crop Breeding and Genetics
- Quantitative Multi-omics to Unravel G2P in Crops and Livestock
- International Centers & Partnerships: Genetic Improvement Resources and Opportunities
- Incorporating Domain Knowledge in Genetic/Genomic Prediction & Analysis Models
- Leveraging Microbiomes in Agriculture

AG2PI
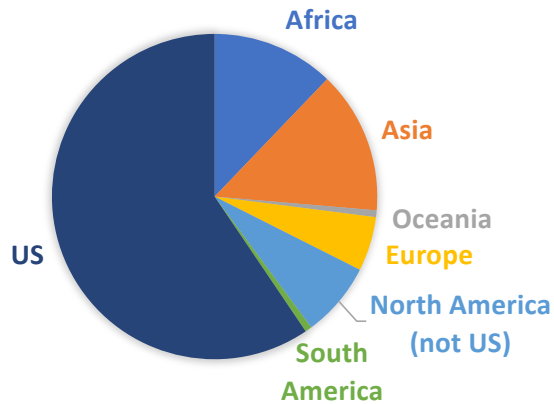Agricultural Genome to
Phenome Initiative

Goals

- Build technical strengths and future collaborative AG2P communities
- Offer a suite of workshops to enable researchers from all backgrounds and computational skill levels to develop best practices, common vocabularies, and technical expertise around genomic and phenomic cyberinfrastructure, data tools and pipelines, statistics, and experimental techniques

Selection of Past Workshop Topics:

- Foundations of Computation: Introduction for Biologists
- Introduction to Scientific Computing
- Unix and Git Skills
- Genotype to Phenotype for Non-Biologists
- Introduction to SNP Data Analysis
- A Guide to GWAS
- Hands-On Machine Learning with Agricultural Applications
- Structural Variant Detection in Animal Populations
- Developing Mobile Computer Vision Applications for Improved Recognition of Livestock
- The APSIM Software Platform to Predict and Explain Genotype x Management x Environment Interactions
- Intermediate Omics Data-Enabled Genomic Prediction and Mediation Analysis

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Agricultural Genome to Phenome Initiative

2022 AG2PI SURVEY RESPONDENTS, BY LOCATION

Africa
Asia
Oceania
Europe
North America (not US)
South America
US

2022 AG2PI SURVEY RESPONDENTS, BY EMPLOYER TYPE

For-Profit Corporation: Established
For-Profit Corporation: Start-Up
Government Agency
University or College
Other
Other Non-Profit Company or Non-Governmental Organization
Producer / Commodity Group
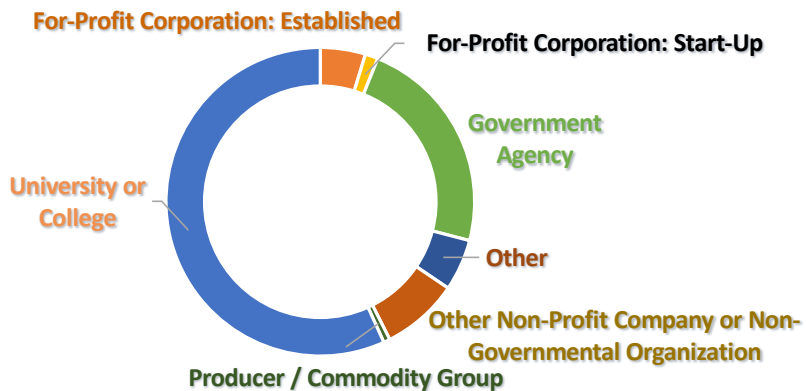
15-question survey
* These topics came from AG2PI Scientific Advisory Board and Steering Committee

Deployed in June of 2022

Purpose: to narrow the scope of future funding to areas that are **most critical** to advancing G2P research as well as those that are **easiest to achieve**

Participants at a September 2022 workshop were asked to rank the same topics and compile survey results

White paper draft based on Sept 2022 Workshop sent to NIFA: "Current Challenges and the Future of Agricultural Genomes to Phenomes in the U.S."

We recommend that AG2PI funding be used to address the following critical milestones:

1. Provide resources to evaluate and **improve Ag G2P predictive tools**, including generation of *benchmark testing datasets*.
2. **Remove current public-private barriers** for collaborating with commercial entities that maintain *large phenotypic datasets*.
3. Establish **a single comprehensive public genome/phenome knowledge base** that enables FAIR data sharing as a foundation for *building on Federal investments* in agricultural genomes.
4. Accelerate the **training of scientists required for agricultural G2P research,** including toward developing and evaluating *data analytics training programs*.
5. Expand the **diversity of people engaged in agricultural G2P activities**, including *researchers, students and producers*.
6. **Identify additional gaps** in knowledge, multidisciplinary team development, education/training, and analytical or quantitative methods relevant to agricultural G2P and *initiate actions to fill those gaps*.

Send your thoughts and suggestions to AG2PI!

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Goals

- Bring people together to develop a vision for the future of Ag G2P and build community

- Identify opportunities and resources within the crop and livestock communities

- Support discussions across research and stakeholder communities

- Communicate and disseminate findings

- Develop white papers to inform USDA NIFA towards future AG2P research and development

Past Conferences:

- Seed Grant mini-conferences

- Listening Sessions at national meetings

- Sept. 22 Conference/Workshop:
"Thinking Big: Visualizing the Future of AG2PI"

White Paper

Future Conference:
- 2023: June 15-16, Kansas City MO
- Mark your calendars and register!
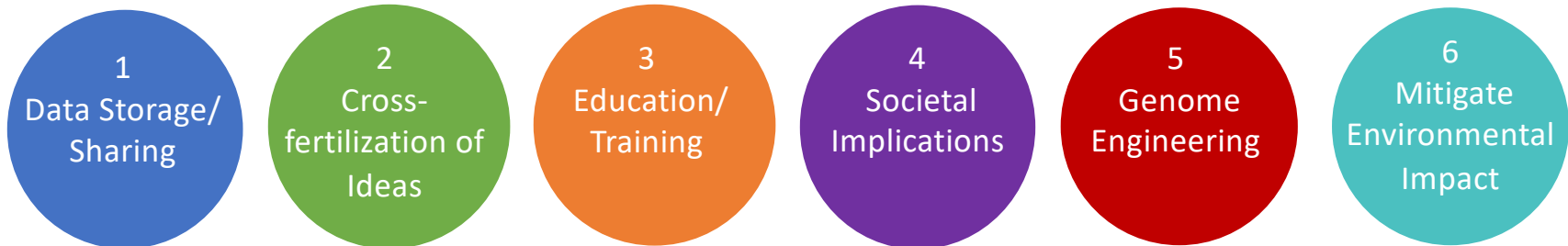
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Project Summary | People | Institutional Involvement | Get Involved | Workshops & Activities | Seed Grants RFP | Publications | Community Surveys | Community Events | Resources | Contact Us

AG2PI
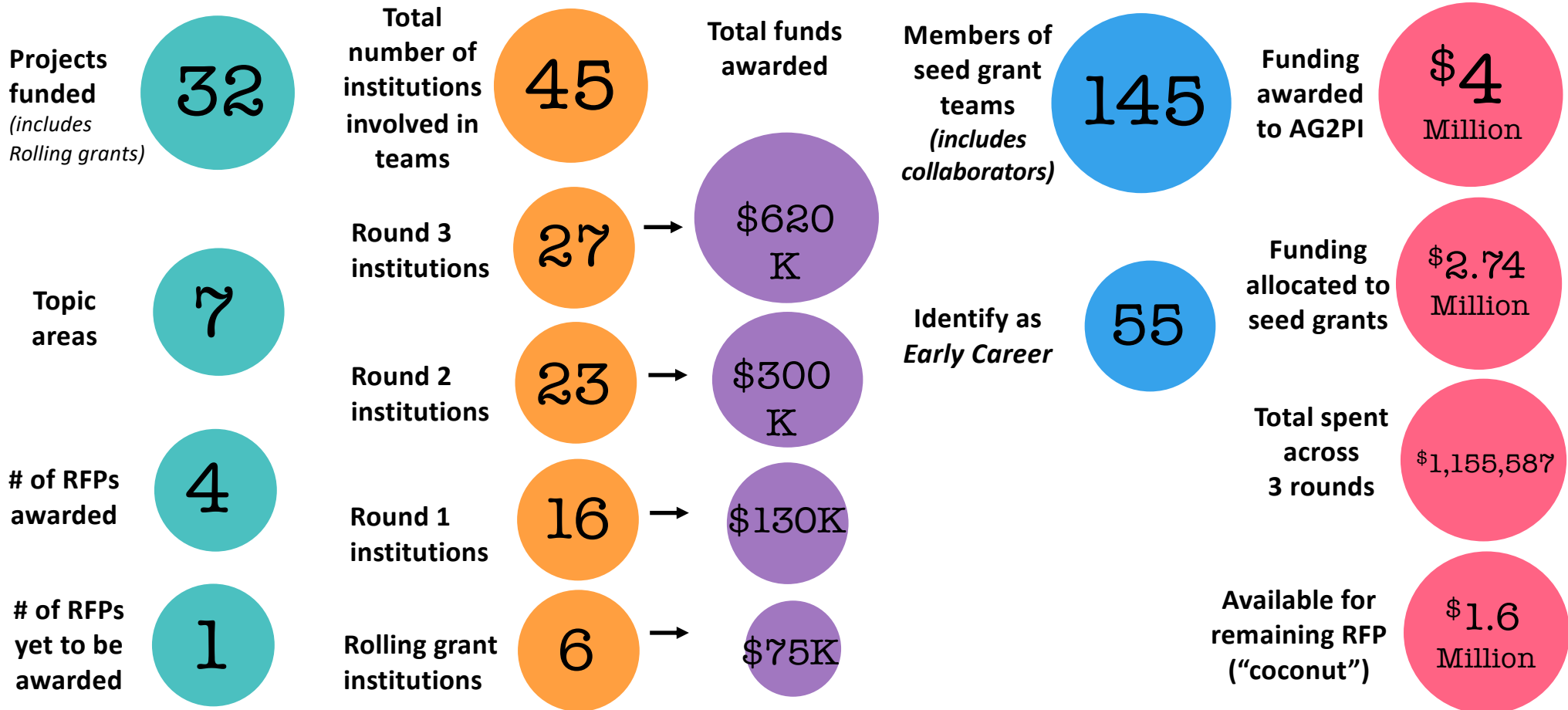Agricultural Genome to
Phenome Initiative

Goals

- Promote collaboration and support the development and cross-pollination of tools, data, and ideas to enable and facilitate future AG2P research
- Foster first steps towards the development of community solutions
  - Research needs and opportunities, physical infrastructure needs, promote capabilities in data processing, analysis and management

Focus areas funded

| 1 Data Storage/ Sharing | 2 Cross-fertilization of Ideas | 3 Education/ Training | 4 Societal Implications | 5 Genome Engineering | 6 Mitigate Environmental Impact |

Seed Grants Overview – By the Numbers

AG2PI
Agricultural Genome to Phenome Initiative

Projects funded *(includes Rolling grants)* — **32**

Total number of institutions involved in teams — **45**

Total funds awarded

Members of seed grant teams *(includes collaborators)* — **145**

Funding awarded to AG2PI — **$4 Million**

Topic areas — **7**

Round 3 institutions — **27** → **$620 K**

Identify as *Early Career* — **55**

Funding allocated to seed grants — **$2.74 Million**

# of RFPs awarded — **4**

Round 2 institutions — **23** → **$300 K**

Total spent across 3 rounds — **$1,155,587**

# of RFPs yet to be awarded — **1**

Round 1 institutions — **16** → **$130K**

Rolling grant institutions — **6** → **$75K**

Available for remaining RFP ("coconut") — **$1.6 Million**

How Can ASAS members participate in AG2P?
$2.5 Million will be in new RFA...

Develop a Vision → Congress wants this from the community (us)
- Identify the research and/ or physical infrastructure needs and opportunities

Develop Community Solutions → Congress wants this too!
- Identify the key components (tools, people, sensors, etc.) necessary for success
- Identify a list of priorities and potential path(s) forward

Working Groups
- Consider working with others to form or participate in a working group

Further ideas on ASAS Participation in AG2PI

- What is important to animal agriculture G2P research?

- What do our respective stakeholders need to make genetic progress in a changing environment?

- How can we work with others to expand what we can deliver?

- How can we help inform NIFA as they establish a new competitive grant program to support research the area of AG2P importance to US agriculture?

- U.S. Congress appropriated **$2,500,000 in fiscal year 2023** for AG2PI, *RFA to be released soon*.

AG2PI
Agricultural Genome to Phenome Initiative

Executive Board Members

Dr. Patrick Schnable
Iowa State University
Principal Investigator

Dr. Jennifer C...
University of Nebra...

...ack Dekkers
...ate University

Dr. David Ertl
Iowa Corn Promotion Board

Nicole Scott, Ph.D.
Project Manager
Iowa State University

Dr. Carolyn Lawrence-Dill
Iowa State University

Dr. Eric Lyons
University of Arizona

Dr. Brenda Murdoch
University of Idaho

Dr. Chris Tuggle
Iowa State University

Introduction to *F*unctional *A*nnotation of *AN*imal *G*enomes (FAANG)-- Goals and Opportunities

Organic growth of FAANG during 2014-2022 Current FAANG

contributors= 571 (Feb 2023)

Join FAANG (it's free!)
Visit: **www.faang.org**

Email us:
faang@iastate.org

authors

Biology 2015

March 2019 membership map

Recent Reviews: Giuffra & Tuggle, *Ann Rev Anim Biosci.* 2018
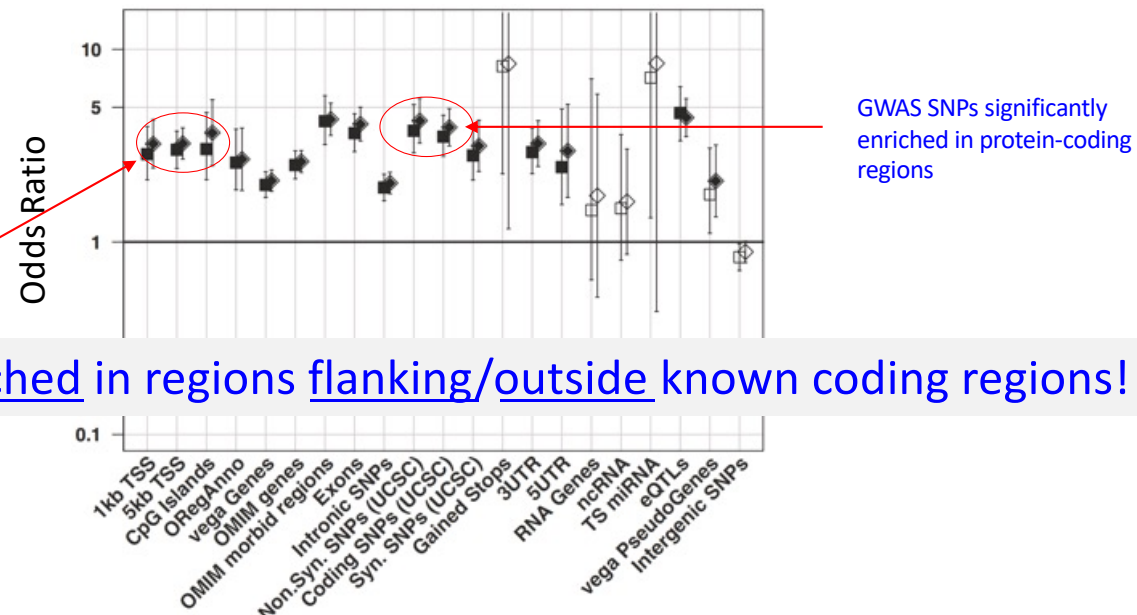Clarke et al. *Genome Biol.* 2020

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 → most important SNP to select for (against)?*

Beyond protein-coding part of genome

Is trait-associated genetic variation located (<u>enriched</u>) in genes?

Yes!

GWAS SNPs significantly enriched in protein-coding regions

But also <u>enriched</u> in regions <u>flanking/outside</u> known coding regions!

Thus we need to *annotate the function* of the ENTIRE genome of our animals

The genomic signature of trait associated variants

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

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):
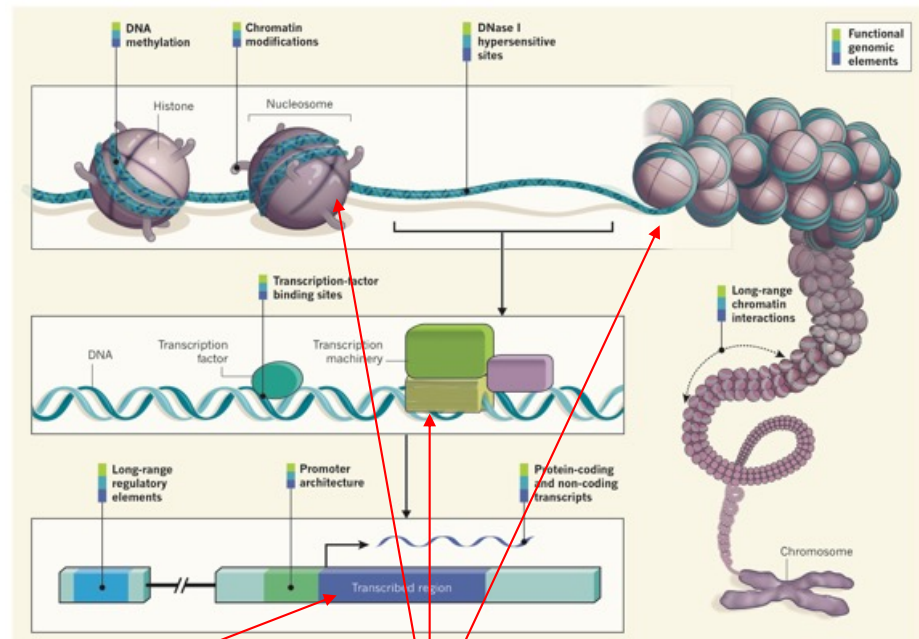
RNA levels and location

Biochemical assays of Chromatin structure

FAANG
Functional Annotation of Animal Genomes

Combinations of signals from different chromatin modifications predict genome function

Jiang, S and Mortazavi, A. 2015 . Briefings in Functional Genomics, 17(2), 2018, 104–115
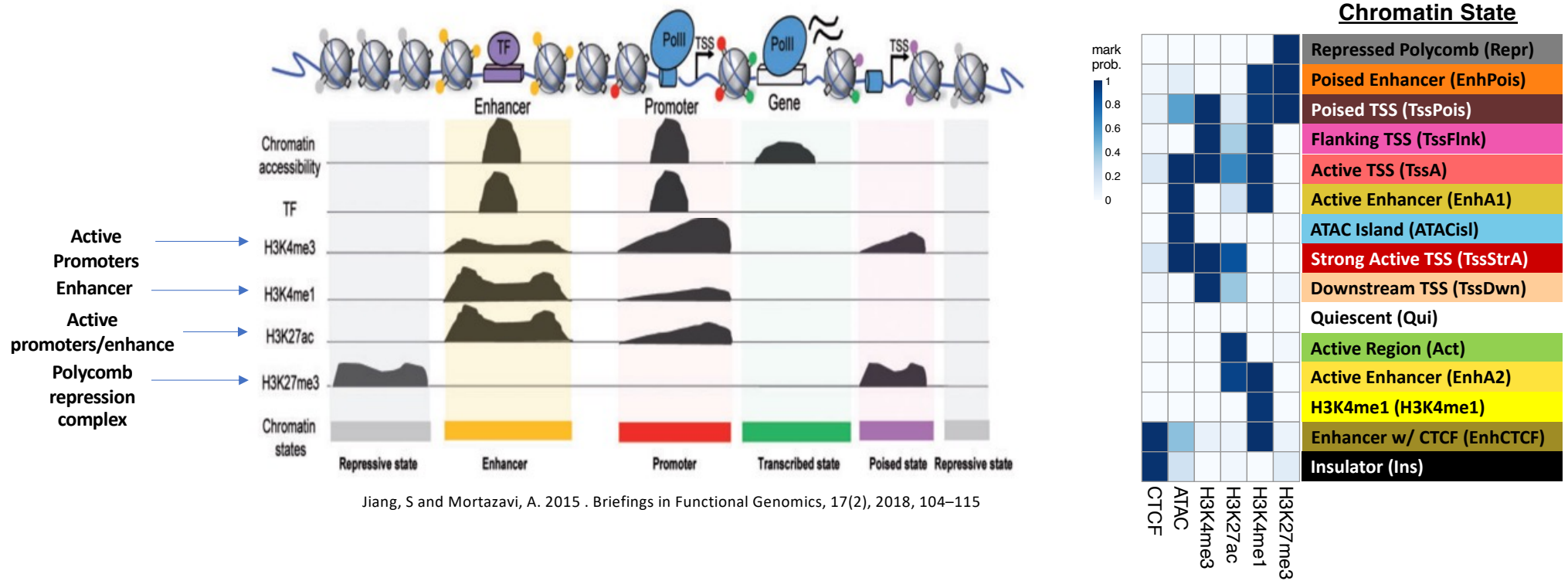
Research on Livestock functional genomics

- National Porcine FAANG project funded by NIFA-AFRI
  - *USDA Center of Excellence- headquartered at ISU*
- One of three funded by USDA (also bovine, chicken) in 2018
- Sheep, horse, aquaculture also funded in recent years
- Large EU projects funded in 2019
  - Monogastrics (Swine+chicken)
  - Bovine
  - Aquaculture
- ***More than $40 Million awarded world-wide for FAANG research***

FAANG
Functional Annotation of Animal Genomes

Functional Annotation of the Porcine Genome

- ***Overall goal:*** *catalog functional elements in the porcine genome for >40 biological states, create Chromatin state map*

Aim 1 Adult tissues

- extend FAANG pilot of 8 -> 25 tissues

Aim 2 Fetal tissues

- Identify and correlate allele-specific expression and AS chromatin modification
- Parent-of-origin effects (reciprocal crosses Meishan x WhiteCross)

Aim 3 Immune System

- Stimulated macrophages and PBMC
- Single cell analysis of blood PMBC and immune tissues
- Circulating Blood Cells- flow-sorted into functional types

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.

FAANG
Functional Annotation of Animal Genomes

Aim 1: Adult tissues *(UC-Davis)*

- extend FAANG pilot of 8 -> 26 tissues

Liqi An, Ying WANG, Claire PROWSE-WILKINS, Huaijun ZHOU, Zhangyuan PAN, Dailu GUAN
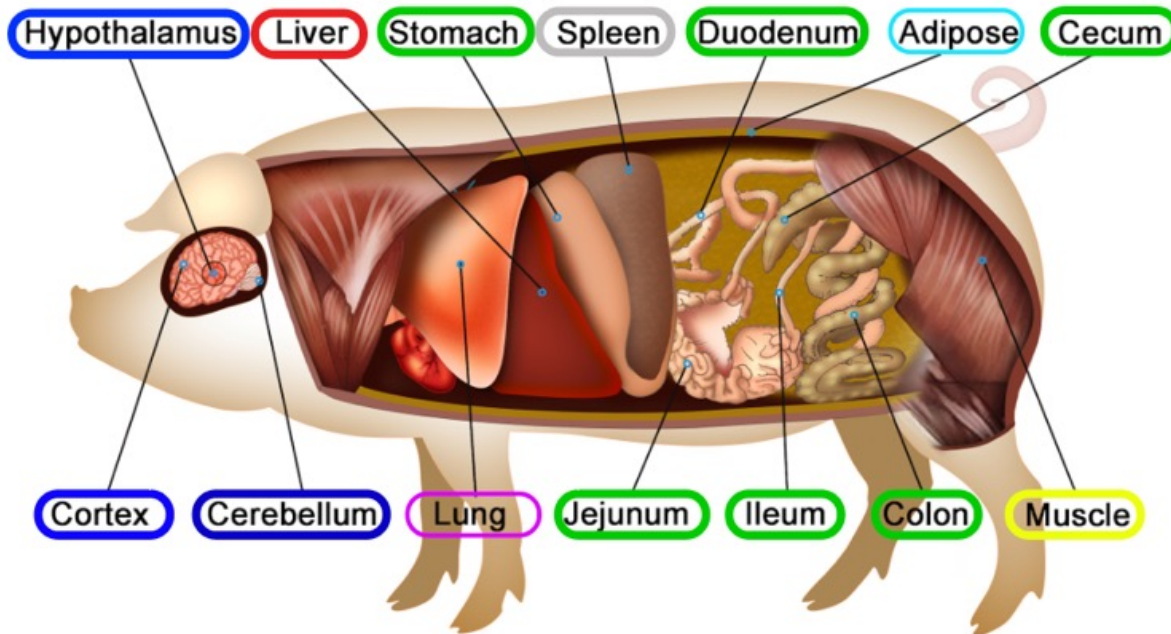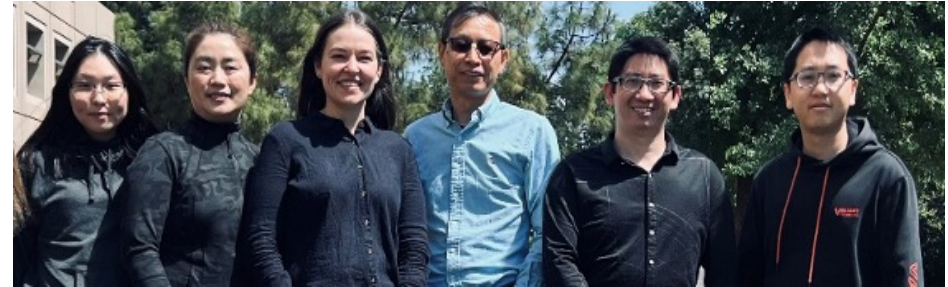
Finished

Core tissues (8): cortex, cerebellum, hypothalamus, liver, lung, spleen, and adipose muscle (Kern, et. al., Nat Commun 2021).

Gut-associated tissues (6): stomach, duodenum, jejunum, ileum, cecum, colon (Pan Z. et al. Nat Commun 2021).
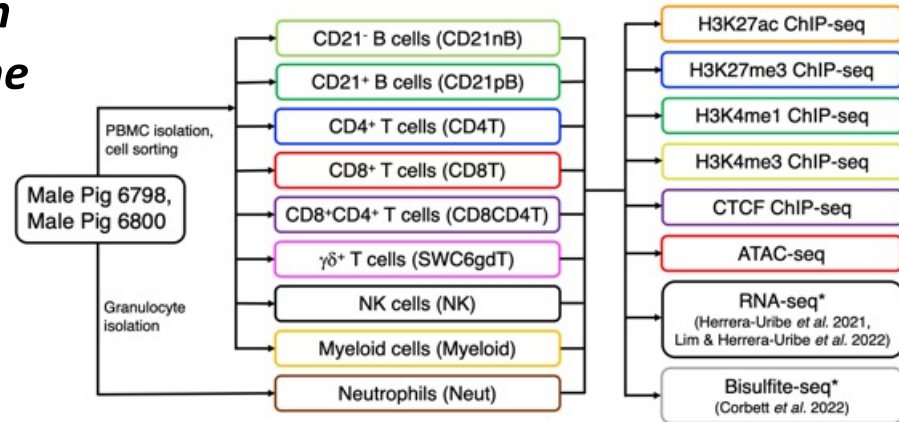
Ongoing:

Remaining adult tissues (12)

Hypothalamus · Liver · Stomach · Spleen · Duodenum · Adipose · Cecum

Cortex · Cerebellum · Lung · Jejunum · Ileum · Colon · Muscle

Aim 3: Functional Annotation of Circulating Porcine Immune Cell Populations

Published:

Herrera-Uribe et al. 2020

Herrera-Uribe & Wiarda 2021

Corbett et al. 2022
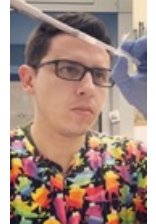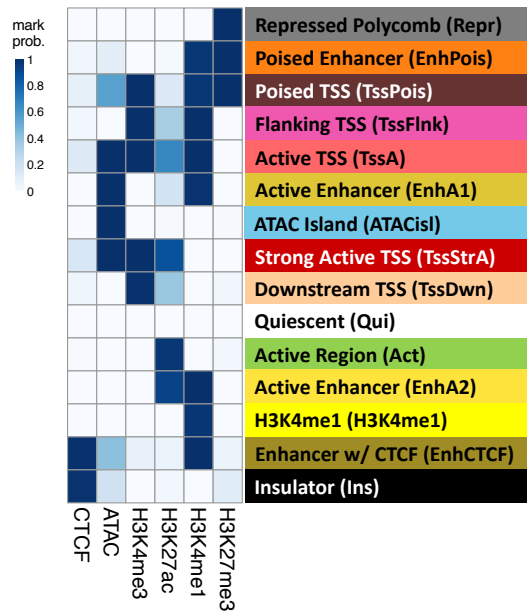

Ryan Corbett   **Juber Herrera Uribe**

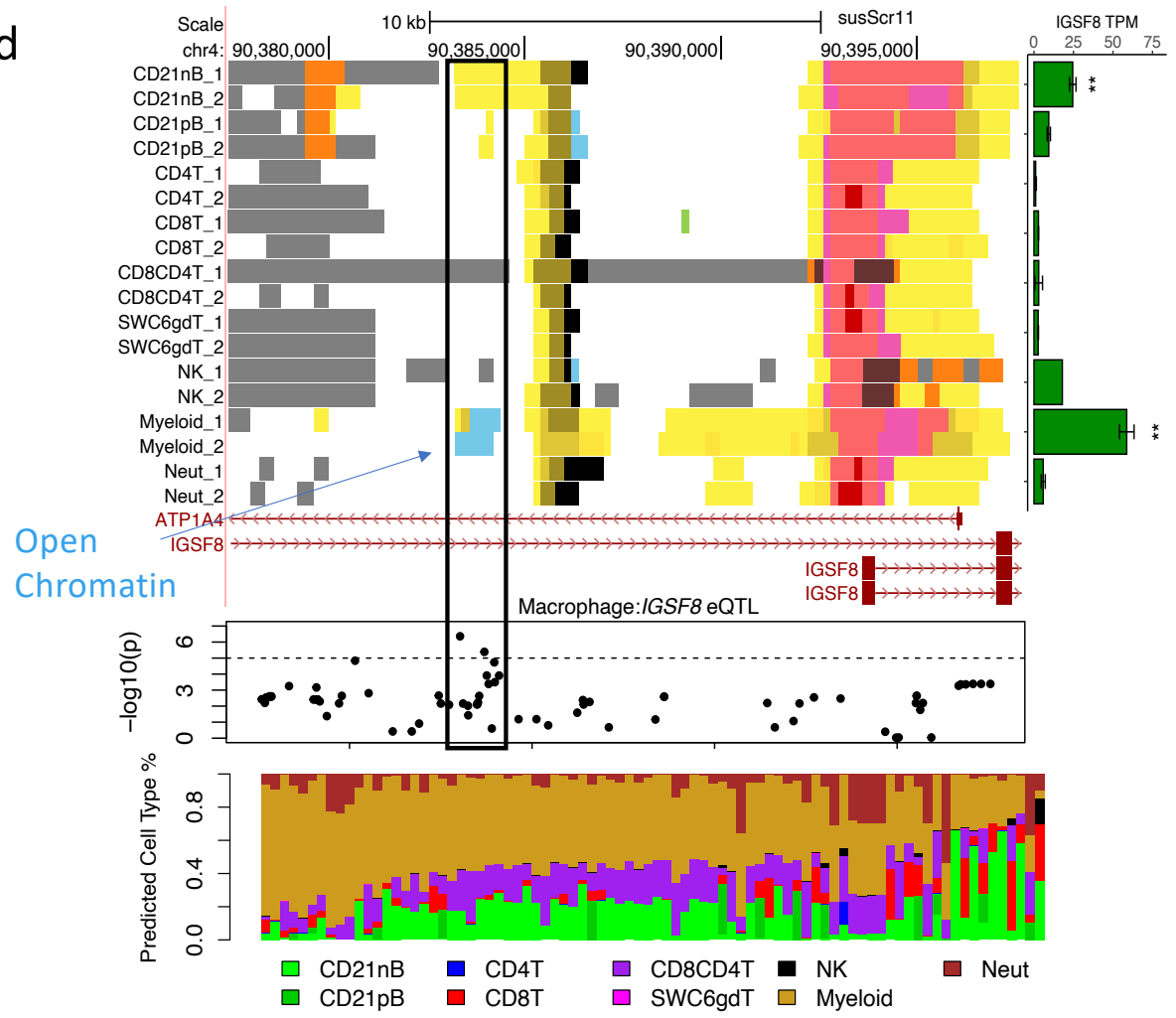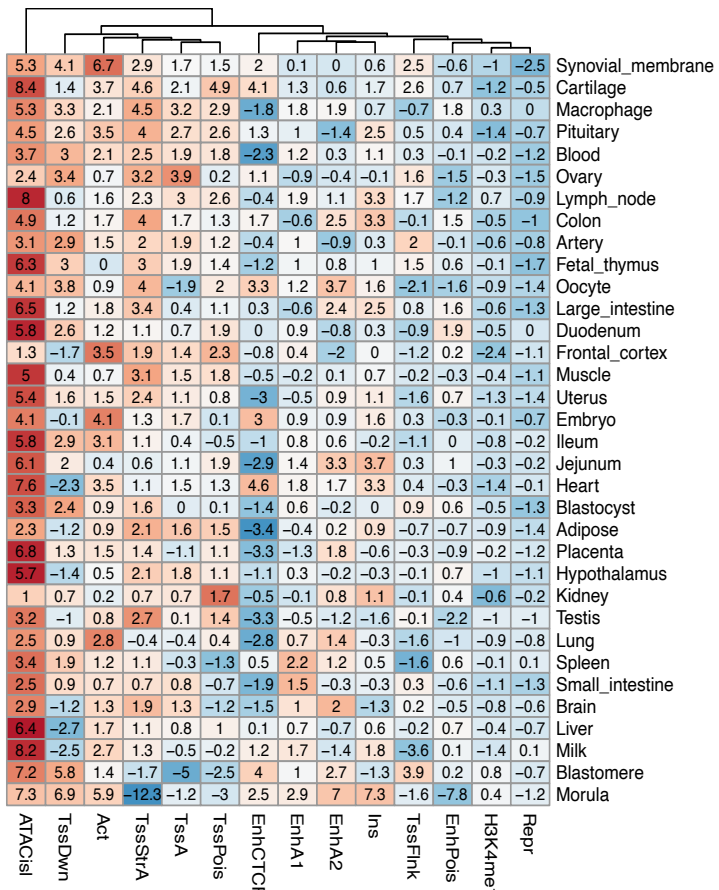**Collaboration:**
Lingzhao Fang, et al. Aarhus U
Crystal Loving, USDA-NADC
Cathy Ernst, Michigan State
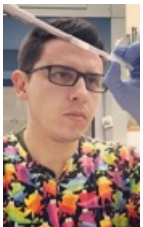
Chromatin State

Active chromatin states are enriched for Pig GTEx eQTL in many tissues

Acknowledgments- FAANG and PIGGI@iastate.edu group
(that's Pig ImmunoGenomics and Genetics in Iowa!)

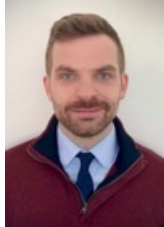Christopher Tuggle

Juber Herrera Uribe
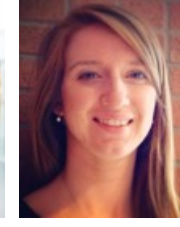
Haibo Liu

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Sathesh Sivasankaran

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IOWA STATE UNIVERSITY

USDA Agricultural Research Service

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UC DAVIS UNIVERSITY OF CALIFORNIA

Huaijun Zhou, et al.

MICHIGAN STATE UNIVERSITY

Cathy Ernst, et al.

USDA Agricultural Research Service

Tim Smith, Dan Nonneman MARC

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FAANG Functional Annotation of Animal Genomes

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