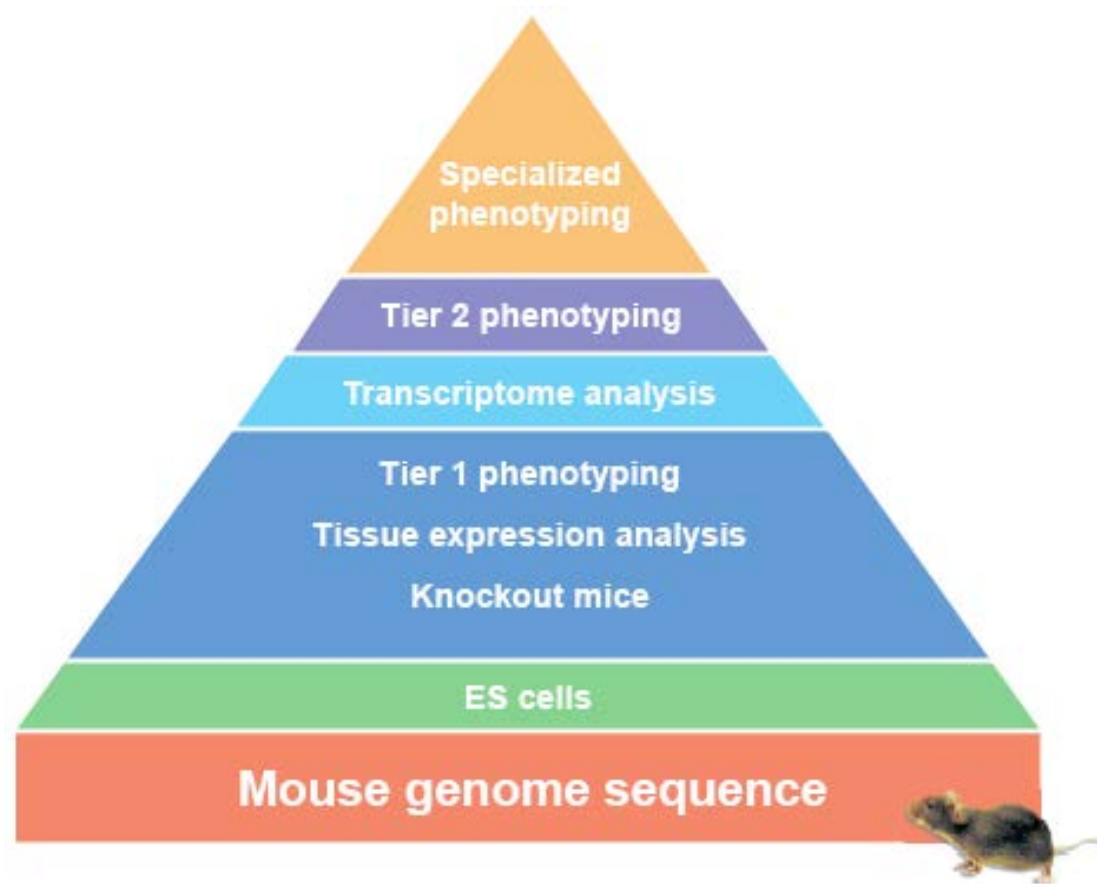


KOMP

THE VISION AND THE FUTURE

Council of Councils

5-2017



The vision for KOMP was articulated in a meeting at the Banbury Center, Cold Spring Harbor in 2003, calling for high throughput production of gene knockouts, and phenotyping, for every gene in the mouse genome.

Scientific Rationale

- Provides access to unannotated genes by providing hypothesis testing and tools
- Provides new insights into pleiotropy

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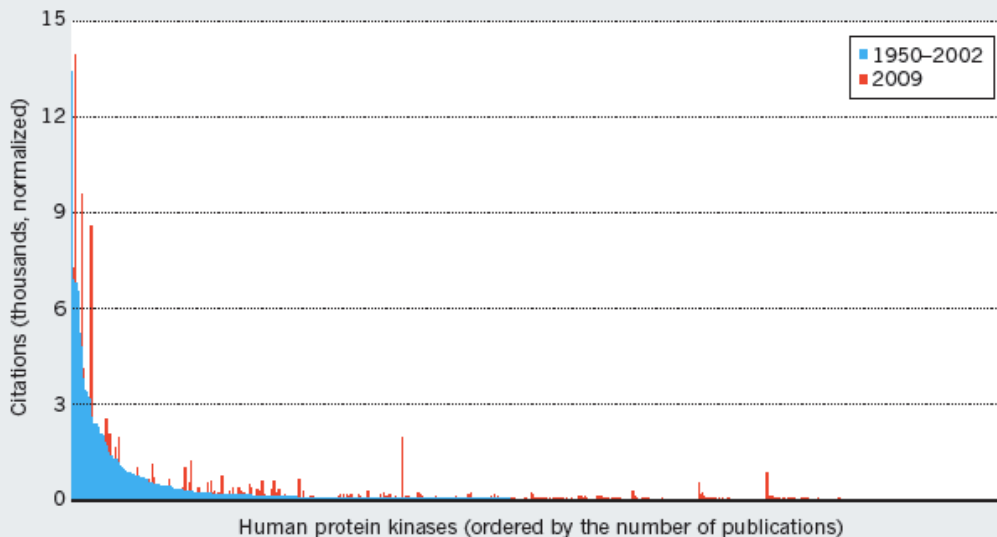
Nature Commentary

Too many roads not taken

Most protein research focuses on those known before the human genome was mapped. Work on the slew discovered since, urge **Aled M. Edwards** and his colleagues.

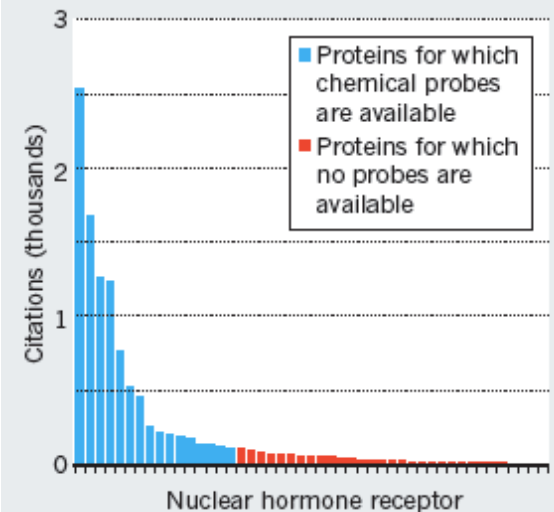
FONDLING OUR PROBLEMS

Researchers' 'favourite kinases' have remained the same for decades with a few exceptions (kinases linked to diseases of great interest to industry).



TOOLS ARE TELLING

The availability of research tools influences a protein's popularity.



Scientific Rationale

- Provides access to unannotated genes by providing hypothesis testing and tools

Genome-wide Generation and Systematic Phenotyping of Knockout Mice Reveals New Roles for Many Genes

White et al., *CELL* 154, 452-464, July 2013

aim of knocking out all genes and screening each line for a broad range of traits. We found that hitherto unpublished genes were as likely to reveal phenotypes as known genes, suggesting that novel genes represent a rich resource for investigating the molecular basis of disease. We found many unexpected phenotypes detected only because we screened for

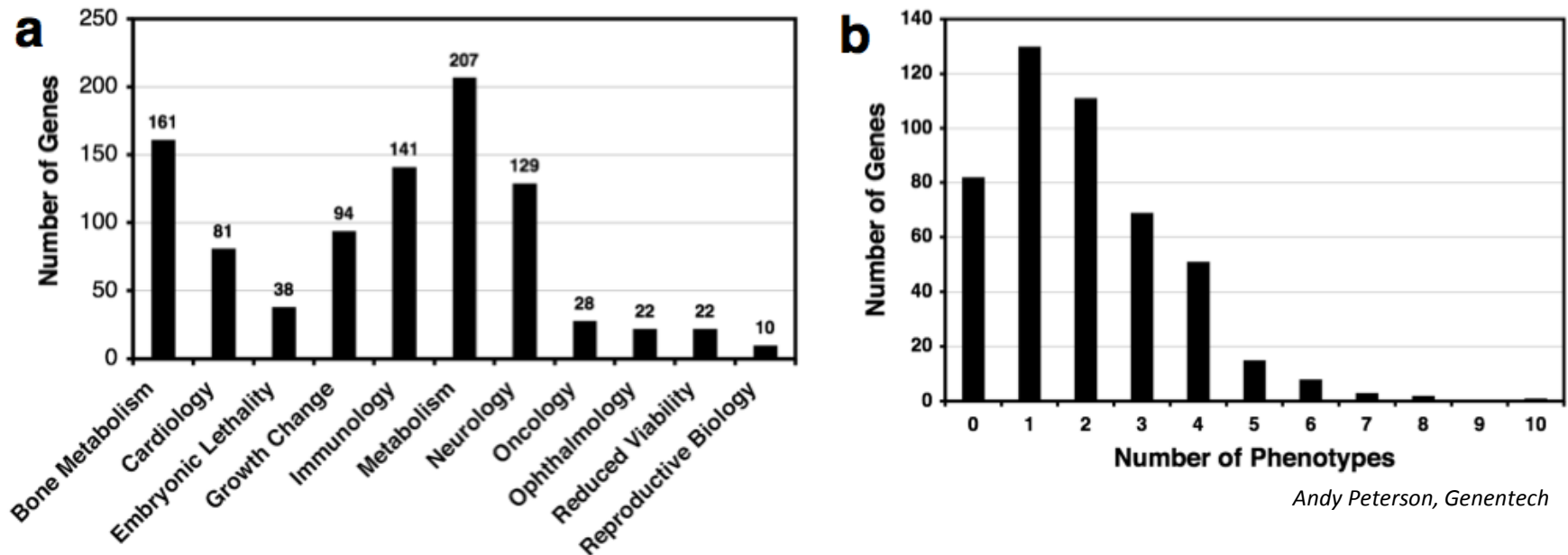
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472 Mouse knockouts were broadly phenotyped



130 (27%) strains had 1 phenotype

245 (52%) strains had 2-5 phenotypes

Policy Rationale

- Eliminates duplication and waste
- Sets the standard for reproducibility
- Includes sex as a biological variable

Policy Rationale

- Eliminates duplication and waste

There has been **extensive** retargeting of mouse genes

Sharing has been very limited

As of 2005, 4848 unique targeted and/or trapped genes revealed that 2655 lines were re-targeted and 702 were targeted greater than 3 times. Even though these are published KOs, only 584 unique genes were in repositories (12%). In summary, each KO is targeted twice on average, and lack of sharing is a common complaint.

To enforce sharing and thereby eliminate retargeting, the community endorsed “repatriation” of published KOs into repositories –

- The Deltagen/Lexicon Repatriation Project

- The KOMP60 Repatriation effort

- The BP/AI Repatriation effort

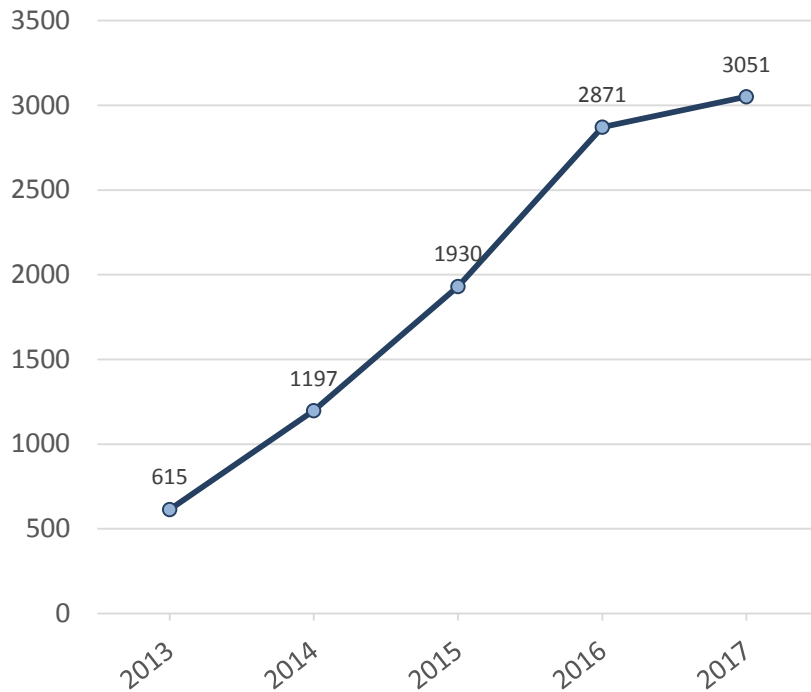
- The KOMP Sharing Plan

- The Cryopreservation supplement effort

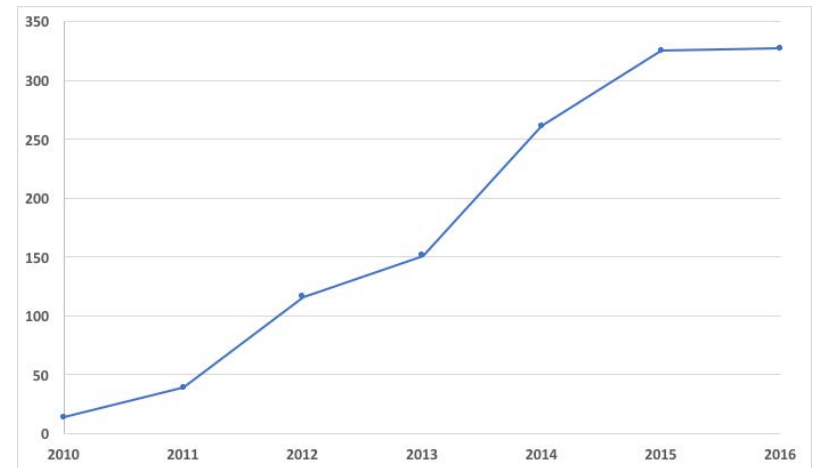
Policy Rationale

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Orders of KOMP2 mice



Publications



1,265 Confirmed Publications

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NATURE | COMMENT

PERSPECTIVE



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Applying the ARRIVE guidelines to an *in vivo* database.

ARRI

Authors

Natasha A. Karp^{*1}, Terry F. Meehan², Hugh Morgan³, Jeremy C. Mason², Andrew Blake³,
Natalja Kurbatova², Damian Smedley¹, Julius Jacobsen¹, Richard F. Mott⁴, Vivek Iyer⁵, Peter
Matthews⁵, David G. Melvin¹, Sara Wells³, Ann M. Flenniken⁶, Hiroshi Masuya⁷, Shigeharu

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Allele - $Eps8l1^{tm2b(KOMP)Wtsi}$

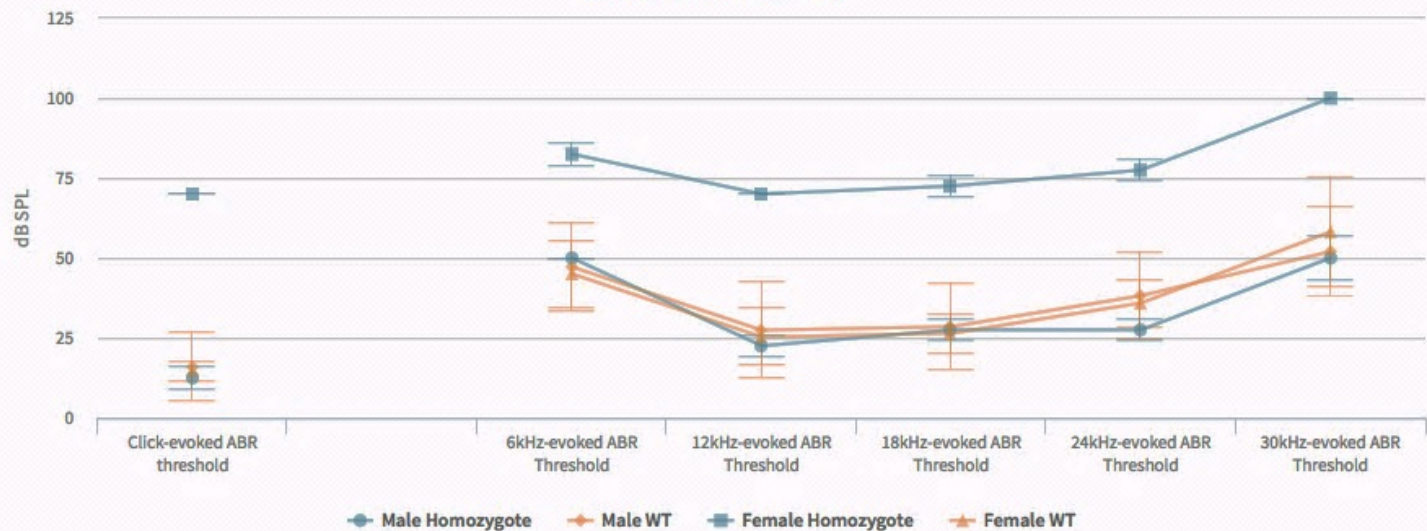
Background - involves: C57BL/6NCrl

Phenotyping Center - UC Davis

Pipeline - [UCD Pipeline](#)

Evoked ABR Threshold (6, 12, 18, 24, 30 kHz)

[Auditory Brain Stem Response](#)



Relevance to Animal Genetics



Arlinda Chief and his *Apaf1* mutation

Identification of a nonsense mutation in APAF1 that is likely causal for a decrease in reproductive efficiency in Holstein dairy cattle. J Dairy Sci. 2016 Aug;99(8):6693-701.

“The reason we had a candidate so quickly was because of the tremendous investment in mouse genetics,” says Lewin.