

“Regardless of whether someone inaccurately believes that a specific breed has a certain behavior or “dangerousness,” a dog with moderate or minor/trace amounts of that breed has the majority of its genome derived from breeds other than the breed in question. It is not rational or scientifically valid to assume that a dog can be defined as dangerous by virtue of having “any element” of a particular breed.” – Dr. Kristopher Irizarry

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**UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF WASHINGTON**

**NICHOLAS CRISCUOLO, individually;
and TAXPAYERS OF THE CITY OF
MOSES LAKE ex rel. NICHOLAS
CRISCUOLO;**

Plaintiff,

vs.

GRANT COUNTY, et al.,

Defendants.

Case No.: CV-10-470-LRS

**PLAINTIFF'S FRCP 26(A)(2)
DISCLOSURE:**

Report of Dr. Kristopher Irizarry

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FRCP 26(a)(2)(B)(i): Complete Statement of All Opinions

1. I have been asked to give an expert opinion concerning (1) whether dog breeds were selected for specific behaviors or, rather, for anatomical, physical, and morphological traits, (2) whether dogs of the same breed exhibit the same behaviors, (3) whether animal control officer, police officer, veterinary school, or dog obedience training produces individuals competent to accurately visually identify dog breeds in mixed breed dogs, (4) whether mixed breed dogs exhibiting a subset of a breed's conformation/physical traits would be expected to exhibit the same behavior as that breed; (5) whether dangerous or hazardous dogs can be identified by breed; (6) whether the methodology (or lack thereof) utilized by the City of Moses Lake in enforcing MLMC 6.06.010(A)(3) is arbitrary, capricious, unreasoning, and not based on sound

IRIZARRY REPORT - 1

ANIMAL LAW OFFICES OF

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1 scientific principles; and related issues.

2 2. In addition to the documents reviewed as stated below, I depend on the professional
3 literature in the sciences of genetics, genomics, neurobiology, neuroscience and veterinary
4 medicine. It is this body of empirical research and theory that informs my professional opinions:

- 5 • Linkage and segregation analysis of black and brindle coat color in domestic dogs. Kerns
6 JA, Cargill EJ, Clark LA, Candille SI, Berryere TG, Olivier M, Lust G, Todhunter RJ,
Schmutz SM, Murphy KE, Barsh GS. *Genetics*. 2007 Jul;176(3):1679-89.
- 7 • Coat variation in the domestic dog is governed by variants in three genes. Cadieu E, Neff
8 MW, Quignon P, Walsh K, Chase K, Parker HG, Vonholdt BM, Rhue A, Boyko A,
Byers A, Wong A, Mosher DS, Elkahlon AG, Spady TC, André C, Lark KG, Cargill M,
9 Bustamante CD, Wayne RK, Ostrander EA. *Science*. 2009 Oct 2;326(5949):150-3.
- 10 • The long and the short of it: evidence that FGF5 is a major determinant of canine 'hair'-
11 itability. Housley DJ, Venta PJ. *Anim Genet*. 2006 Aug;37(4):309-15.
- 12 • Genome sequence, comparative analysis and haplotype structure of the domestic dog.
13 Lindblad-Toh K, Wade CM, Mikkelsen TS, Karlsson EK, Jaffe DB, et al. *Nature*. 2005
14 Dec 8;438(7069):803-19.
- 15 • A single IGF1 allele is a major determinant of small size in dogs. Sutter NB, Bustamante
16 CD, Chase K, Gray MM, Zhao K, Zhu L, Padhukasahasram B, Karlins E, Davis S, Jones
17 PG, Quignon P, Johnson GS, Parker HG, Fretwell N, Mosher DS, Lawler DF, Satyaraj E,
18 Nordborg M, Lark KG, Wayne RK, Ostrander EA. *Science*. 2007 Apr 6;316(5821):112-
19 5.
- 20 • Inbreeding and genetic diversity in dogs: Results from DNA analysis. Wade CM. *Vet J*.
21 2011 Aug;189(2):183-8. Epub 2011 Jul 13.
- 22 • A mutation in the myostatin gene increases muscle mass and enhances racing
23 performance in heterozygote dogs. Mosher DS, Quignon P, Bustamante CD, Sutter NB,
24 Mellersh CS, Parker HG, Ostrander EA. *PLoS Genet*. 2007 May 25;3(5):e79.
- 25 • A simple genetic architecture underlies morphological variation in dogs. Boyko AR,
Quignon P, Li L, Schoenebeck JJ, Degenhardt JD, Lohmueller KE, Zhao K, Brisbin A,
Parker HG, vonHoldt BM, Cargill M, Auton A, Reynolds A, Elkahlon AG, Castelhana
M, Mosher DS, Sutter NB, Johnson GS, Novembre J, Hubisz MJ, Siepel A, Wayne RK,
Bustamante CD, Ostrander EA. *PLoS Biol*. 2010 Aug 10;8(8):e1000451.
- Relationships between gene expression and brain wiring in the adult rodent brain. French
L, Pavlidis P. *PLoS Comput Biol*. 2011 Jan 6;7(1):e1001049.
- An anatomic gene expression atlas of the adult mouse brain. Ng L, Bernard A, Lau C,
Overly CC, Dong HW, Kuan C, Pathak S, Sunkin SM, Dang C, Bohland JW, Bokil H,

1 Mitra PP, Puelles L, Hohmann J, Anderson DJ, Lein ES, Jones AR, Hawrylycz M. *Nat*
2 *Neurosci.* 2009 Mar;12(3):356-62.

- 3 • Comparison of Adoption Agency Breed Identification and DNA Breed Identification of
4 Dogs. Voirth VL, Ingram E, Mitsouras K, Irizarry K. *J. App. Animal Welfare Sci.* 12:3,
5 253-262 (2009).

6 My opinions are also widely accepted by virtually all experts in the fields of genetics and
7 neurobiology. I am not aware of any dispute, much less a significant one, by qualified experts in
8 these germane scientific communities concerning the theories and methodologies employed by
9 me in drawing these conclusions.

10 3. With a level of confidence beyond reasonable scientific certainty and evidentiary
11 preponderance, and based on my training, familiarity with professional literature, and
12 experience, implementing well-grounded and generally accepted methodologies and theories, I
13 reach the following expert conclusions:

14 (1) Dog breeds have been selected and differentiated based on anatomical features.

15 (2) Anatomical features associated with dog breeds are found in many different breeds.

16 (3) AKC dog breeds are defined through a closed breeding pool.

17 (4) Dog breeds can be defined at the genetic level as lacking genetic variation in some
18 regions of the genome, i.e., German Shepherds lack the genetic variants associated with the very
19 short snout found in the French Bull dog.

20 (5) A mixed breed dog is not a member of a breed.

21 (6) The defining anatomical features of dog breeds are the result of a handful of genes
22 that have been identified and listed in peer-reviewed scientific publications.

23 (7) The anatomical features associated with dog breeds do not encode the brain or the
24 connections of brain cells and are not involved in encoding the behavior of a dog.

1 (8) Unlike identical twins in humans – who have identical DNA, members of dog breeds
2 may look the same and have very different DNA.

3 (9) Dogs with open breeding pools, such as mixed breed dogs, cannot be considered a
4 member of a specific breed.

5 (10) A dog that is 25% Labrador Retriever is not eligible to compete in an AKC dog
6 show for Labrador Retrievers.

7 (11) Visual identification of dog breeds is inaccurate.

8 (12) Visual identification of dog breeds differs from DNA identification of dog breeds.

9 (13) The lack of efficacy in identifying dog breeds is the result of relatively few regions
10 of the genome being associated with anatomical traits.

11 (14) Moses Lake’s approach to identifying dog breeds in mixed breed dogs based upon
12 visual inspection for particular anatomical features is not scientifically valid.

13 (15) The anatomical similarity of dogs within a breed causes people to assume that dogs
14 within a breed share other traits, such as behavior, health and disease susceptibility, yet this
15 assumption is flawed.

16 (16) There is no scientific basis for better-than-chance visually accurate breed
17 identification by animal control officers and does not meet the *Frye* or *Daubert* test for
18 admissibility.

19 (17) Animal professionals, including veterinarians, dog breeders, dog show judges,
20 animal control officers and others are not capable of accurately identifying breeds in mixed breed
21 dogs.

22 (18) The manner in which mixed breed dogs are visually identified is so subjective as to
23 be arbitrary and capricious.

1 (19) Santiago Reyna has made identifications, but has never confirmed that his
2 identifications are correct by independent, scientifically valid corroborating evidence. Thus, the
3 accuracy is unknown, untested and unscientific. This is underscored by the fact that Dymond was
4 not identified as hazardous in a photo seen by Ofc. Reyna during deposition.

5 (20) An "element" is undefinable in terms of mixed dog breeds.

6 (21) Even using DNA, an "element" is vague and unable to be intelligently applied since
7 all dogs share 99.9975% of their DNA across breeds.

8 (22) An element cannot be reliably visually identified in a mixed breed dog.

9 (23) An element of a mixed breed dog identified visually by Ofc. Reyna does not
10 scientifically or rationally ensure the presence of one of the prohibited breeds under MLMC
11 6.06.010(A)(3).

12 (24) The notion that the presence of an anatomical feature, i.e., smooth coat, correlates
13 with behavior is not rational.

14 (25) Visual identification of mixed breed prohibited dogs under MLMC 6.06.010(A)(3)
15 does not reliably or rationally meet the purported goals of Ch. 6.06 MLMC (i.e., to ensure that
16 dogs are classified accurately and banished or euthanized to protect the public safety).

17 (26) Breed bans do not work because bite rates do not go down; thus, there is no rational
18 basis in terms of increasing public safety.

19 (27) There is no scientific evidence that the breeds listed in MLMC 6.06.010(A)(3) are
20 more aggressive or dangerous than other dogs. This is due, in part, to the problem of acquiring
21 accurate statistics on the total number of dogs. N.B.: the CDC specifically stated that its fatal
22 study was not to be used for breed bans.

23 (28) Since studies regarding breeds and bites rely in the end on visual identification by
24

lay people, they are totally inaccurate and unscientific.

(29) The science of dog DNA is the most accurate method to determine mixed breed dogs and will supplant visual identifications.

(30) Most people erroneously believe that dog breeds were bred for specific behaviors. This is a stereotype unsupported by the recent scientific findings that identify anatomical traits as the foundation of breed stratification.

(31) Most people erroneously believe that a mixed breed dog that contains an anatomical component in common with a specific breed must be a member of that breed. However, by definition, a mixed breed dog is not a member of a specific dog breed.

(32) The stratification of dogs into breeds reduces the genetic variation within a breed. Once a member of the breed is crossed with other breeds of dogs, it gains the genetic variation from these other dogs and loses the genetics associated with a single breed.

(33) Regardless of whether someone inaccurately believes that a specific breed has a certain behavior or “dangerousness,” a dog with moderate or minor/trace amounts of that breed has the majority of its genome derived from breeds other than the breed in question.

(34) It is not rational or scientifically valid to assume that a dog can be defined as dangerous by virtue of having “any element” of a particular breed.

(35) The visual identification of dogs has been used to identify the dangerousness of specific breeds historically. My review of this practice leads me to conclude, however, that whatever breed is arbitrarily defined as dangerous gets blamed for dog bites by the media. Furthermore, none of the mixed breed dogs previously involved in dog bites have been accurately assessed for breed composition.

(36) The notion that any element of some breed would make a dog dangerous is not

1 rational and metaphorically akin to stating that “any car that has the same color as a car driven by
2 a drunk driver is a dangerous car.”

3 (37) Incorporating by reference attached exhibits.

4 **FRCP 26(a)(2)(B)(ii): Facts or Data Considered in Forming Opinions**

5 4. I have reviewed the following materials in arriving at my opinion: *Deposition of Dean*
6 *Mitchell, Deposition of Santiago Reyna, Answers and Responses to Plaintiff's First Discovery*
7 *Requests to the City of Moses Lake*, public records responses from the City of Moses Lake,
8 genetic breed profiles reported as to specific dogs tested by Mars Veterinary, maker of the
9 Wisdom Panel® Professional Canine Genetic Analysis, which is reasonably relied upon by
10 experts in my fields of expertise in forming opinions and inferences on the subjects herein.

11 **FRCP 26(a)(2)(B)(iii): Exhibits Used to Summarize or Support Opinions**

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13 5. Exhibits used to summarize and support my opinions include those used in the
14 depositions of Mitchell and Reyna, as well as attached.

15 **FRCP 26(a)(2)(B)(iv): Expert Qualifications – List of Publications**

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17 6. The attached curriculum vitae provides my qualifications and list of publications
18 authored by me in the past ten years.

19 **FRCP 26(a)(2)(B)(v): Prior Testimony**

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21 7. In the past four years, I have not testified as an expert at trial or by deposition.

22 **FRCP 26(a)(2)(B)(vi): Compensation**

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24 8. I am charging \$50 per hour to the Plaintiff for my study and testimony in the case,
25 including costs of travel, room, and board. I will charge \$100 per hour, plus costs of travel,

1 room, and board should Defendant depose me or if I am called to testify at trial.

2 9. I reserve the right to amend and change my declaration and expert opinions as I review
3 further evidence presented in this case, including but not limited to depositions and live
4 testimony and FRCP 26(a)(2) disclosures by the Defendant.

5 Executed this Aug 17, 2011 in the city of Pomona, California

6
7 Kristopher Irizarry, Ph.D.
8 KRISTOPHER IRIZARRY, PH.D.

Kristopher J. L. Irizarry, Ph.D.

CURRICULUM VITAE

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Pomona, California 91766-1854

Updated: March 2011

EDUCATION:

B.S. Biochemistry & Biophysics, 1996
Rensselaer Polytechnic Institute, Troy New York

Ph.D. Biochemistry & Molecular Biology, 2003

Dissertation Title “*Identification and Analysis of Single Nucleotide Polymorphisms in the Coding Regions of the Human Genome*” University California, Los Angeles

Postdoctoral Fellowship UCLA Center for Pharmacogenomics
Pharmacogenomics of Antidepressant Treatment Response
Neuropsychiatric Institute, David Geffen School of Medicine at UCLA

PROFESSIONAL EXPERIENCE:

2006 - present Assistant Professor, Bioinformatics, Genetics & Genomics
College of Veterinary Medicine
Western University of Health Sciences
Pomona, California

2004-2005 Lecturer / Researcher
Neuropsychiatric Institute (NPI)
University California, Los Angeles, CA

2003- 2004 Postdoctoral Fellowship Neuropsychiatric Institute (NPI),
University of California, Los Angeles, CA.

2000 Teaching Assistant: Biochemistry and Molecular Biology
University California, Los Angeles, CA

1998-1999 Teaching Assistant: Molecular, Cellular, and Developmental Biology
University of California, Los Angeles, CA

1998-2003 Graduate Student, Laboratory of Bioinformatics & Structural Genomics,
University of California, Los Angeles, CA.

1997 Bioinformatics Research Internship
Incyte Pharmaceuticals
Palo Alto, CA

1995-96 Research Assistant, Center for Biophysics,
Rensselaer Polytechnic Institute, Troy NY

1995 Summer Research Position, NINDS/
National Institutes of Health, Bethesda, MD

1994-95 Research Assistant, Addictions Laboratory, RPI, Troy, NY

PROFESSIONAL ACTIVITIES:

California Veterinary Medicine Association – faculty membership
Evidence Based Veterinary Medicine Association – charter membership
California Science Fair – Judges Advisory Committee
Advisor – Genetics, National Canine Research Council
Coordinator – Western University Students Research and Technology Symposium (STARS)

HONORS AND AWARDS:

2003 – 2004 NIH T32 Psychobiology Postdoctoral Fellowship
2000 - 2003 NSF Integrative Graduate Education and Research Traineeship
1998 - 2000 NIH Biotechnology Training Grant
1994 - 1996 Rensselaer Scholarship

RESEARCH FUNDING:

9/1/08-12/30/11 Research Contract \$19,000
PI: K. Irizarry Hills Pet Nutrition
“Nutrigenomics: comparative genomics analysis of novel gene sequences”

1/1/09 - 12/31/11 USDA \$325,000
“Impact of immune responses of chickens with defined B haplotypes on resistance to respiratory infection” PI: Ellen Collisson, Yvonne Drechsler, **Co-investigators: K. Irizarry**, M Saggese

10/2009-9/2011 Institute of Museum and Library Services \$100,000
“Correlation of Snow Leopard Genetics with Immune Function: A Model for the Integration of Functional Genomics into Endangered Species Captive Breeding Plans.”
IMLS Collaborative Planning Grant
Project Director: Margaret C. Barr; **Co-PIs: Kristopher Irizarry**, Janis Joslin, Collaborators Todd Mockler, Jay Tetzloff

1/1/07-12/30/08 Research Subcontract \$20,000
PI: K. Irizarry Center for Neuroeconomic Studies, Claremont Graduate University
“Analysis of genes associated with behavioral and neuroeconomic phenotypes in humans”

7/1/07 Anonymous Gift value: \$15,000
PI: K. Irizarry hardware donation
“Computational Infrastructure for cluster computing genomics applications”

7/1/2007-6/30/08 Intramural Research Grant \$15,000
PI: K. Irizarry Western University of Health Sciences
“Identification and analysis of genes underlying behavioral phenotypes: combining bioinformatics, comparative genomics and sequencing to accelerate discovery in the canine genome”

9/30/02-9/29/07 NIDDK/NIH \$80,000
PI: Julio Licinio, M.D. R01 DK063240
Co-investigator: Kris Irizarry, Ph.D., awarded a minority supplement for this project.
"Depression and Metabolic Syndrome in Mexican-American Women"

09/28/04-07/31/07 NCRR/NIH \$42,000
PI: Robert M. Bilder 1P20RR020750
Co-investigator: Kris Irizarry, Ph.D
"Cognitive Phenotyping for Neuropsychiatric Therapeutics"

09/30/83-06/30/08 NIMH/NIH \$33,000
PI: Andrew F. Leuchter 5T32MH017140-20
Post-doctoral fellow: Kris Irizarry, Ph.D.
"Research Training: Psychological Sciences"

LECTURES & PRESENTATIONS & POSTERS:

Kristopher Irizarry "Comparative Mammalian Phenomics" *Guest Lecturer at Oregon State University Graduate Course in Genomics*. March 4th and March 7th, 2011

Katherine Mitsouras, Erica A. Faulhaber, Gordon Hui, **Kristopher J. L. Irizarry**. "Development of a PCR-assay to detect papillomavirus in the snow leopard." *Plant and Animal Genomics Meeting*. San Diego, California, January 15-19, 2011

V. Voith, C. Chadik, E. Ingram, **K. Irizarry**, K. Mitsouras, J. Marilo. "Dog Breed Identification". *American College of Veterinary Behaviorists and The American Veterinary Society of Animal Behaviorists* Atlanta, Georgia, 2010

Hui, Erica Faulhaber, Aleli Camacho, Katherine Mitsouras, **Kristopher Irizarry**. "Construction of a Comparative Genomics Map To Facilitate The Annotation Of The Draft Snow Leopard Genome". *Merial Veterinary Scholar's Symposium*, Athens, Georgia, August 2010.

Kristopher Irizarry "How to facilitate student use of published and online resources during creation of science projects" *Presentation for Mentors of California Science Fair Students*, California Science Fair May 2010.

Katherine Mitsouras, Gabrielle Galgoul, Audrey Hoholm, Cheng Li, **Kristopher Irizarry** "Using bioinformatics and comparative genomics to map cancer associated phenotypes to the canine genome." *Genes, Dogs & Cancer: 5th International Canine Cancer Conference* February 13 – 15, 2009, Orlando Florida (submitted abstract was accepted for poster presentation in February 2009)

Irizarry, Kristopher "'The great debate - Does behavioral genetics imply behavior is deterministic? Reflections on free will, determinism and the contributions of nature and nurture to animal behavior" *Western University College of Veterinary Medicine Behavior Club* – Invited Talk – November 2008.

Irizarry, Kristopher "Developing novel comparative genomics based phenotype annotation for use in the publicly available gene expression analysis software package DChip" *Department of Biostatistics and Computational Biology*, Dana Farber Cancer Institute, Harvard University, Boston MA, Oct. 29, 2008.

Irizarry, Kristopher "Bioinformatics and Comparative Genomics Approaches for Annotating The Chicken Genome" *USDA Multistate Immunogenetics Research Poultry Meeting*, October 16 2008, Washington DC.

Irizarry, Kristopher "Leveraging Comparative Genomics to Infer-Functional Consequences of Gene Expression Changes: Accelerating Microarray Discovery via Phenomics Annotation" *Cambridge Healthtech's Eighth Annual Integrative Data Analysis Conference*, Providence Rhode Island, Sept. 24, 2008

V. Voith & **Irizarry, K** “Dog Breed Identification Quiz and DNA results” *Orange Belt Veterinary Medical Association*, Riverside CA - September 16, 2008

Irizarry K “Decoding Dog DNA: finding physiology and pathology in the canine genome” *Western University of Health Sciences Research Seminar*: Pomona, California August 27, 2008

Irizarry, Kristopher “An introduction to the genetics of behavior” *Charles Drew University, Los Angeles California*, August 12, 2008.

Irizarry, Kristopher “Comparative Genomics: From Mice to Men and Dogs” *Western/Drew Research Retreat at the California Endowment Center for Healthy Communities in Los Angeles*. July 15, 2008.

Irizarry, KJ “Managing a collaborative Problem-Based Learning Curriculum” *Lilly-West SoTL Conference*, Pomona California, March 22, 2008

Irizarry K “Understanding canine genetics as it relates to dog breeds and behavior” *Invited Talk for The Farm Animal Foundation*, New York, Oct. 2007

Irizarry KJL, Day A, Mitsouras K, Lee CJ, Wong ML, Licinio J. “Novel Strategies for Psychiatric Pharmacogenomics” *Pharmacogenetics Research and Knowledge Base Fourth Scientific Meeting* Los Angeles, California March 8, 2004.

Irizarry K, Day, A, Mitsouras K, Lee C, Wong ML, Licinio J. “Identification and Integration of Diverse Genomic Signals: Building Neuroinformatics Tools for Pharmacogenomics Applications” *International Society of Pharmacogenomics Meeting* LA, CA Nov. 2003.

Irizarry K, Day, A, Mitsouras K, Lee C, Licinio J. “Identifying candidate SNPs for high-throughput pharmacogenomics studies of CNS disorders” *International Pharmacogenomics Joint Cold Spring Harbor Laboratory/Wellcome Trust Conference*, Hinxton UK Sep. 25, 2003

Irizarry, K, Galbraith, S, Miller, D, Lee, C. “Genomic SNP Mapping” *Lake Tahoe Symposia on Molecular Diversity*, January 29 - February 2, 2001

Lin, XJ, **Irizarry, K.**, Lengyel, JA "Drosophila Arc, a novel membrane associated PDZ domain protein is involved in epithelial morphogenesis" *39th Annual Drosophila Research Conference* Washington D.C. March, 1998

Chambers, M. D., **Irizarry, K. L.**, Boswell, K. J., Hubbell, C. L., & Reid, L. D., “A Selective Opioid Antagonist Block’s Cocaine’s Rewarding Effects” Presented at the *American Psychological Association Annual Conference*, New York, New York, August 1995.

PAPERS - IN REVIEW / PREPARATION

Kristopher J. L. Irizarry, Sukhaswami Malladi, Xiangming Gao, Katherine Mitsouras, Lynda Melendez, Patricia Burris, Jeffrey Brockman, Samer Al-Murrani.
"Sequencing and Comparative Genomic Analysis of 1227 Felis catus cDNA Sequences Enriched for Developmental, Clinical and Nutritional Phenotypes"

manuscript in preparation, anticipated submission for Genome Biology date:
April 15 2011.

Katherine Mitsouras, Erica Faulhaber, Gordon Hui, Janis Joslin, Curtis Eng, Margaret C. Barr, **Kristopher J. L. Irizarry** "Development of a PCR Assay to Detect Papillomavirus Infection in the Snow Leopard" BMC Veterinary Research, submitted Jan. 26, 2011, *under review*

PAPERS – PEER REVIEWED

Liao G, Wen Z, **Irizarry K**, Huang Y, Mitsouras K, Darmani M, Leon T, Shi L, Bi X. Abnormal gene expression in cerebellum of Npc1^{-/-} mice during postnatal development. Brain Res. 2010 Apr 14;1325:128-40.

Voith VL, Ingram E, Mitsouras K, **Irizarry K**. Comparison of adoption agency breed identification and DNA breed identification of dogs. J Appl Anim Welf Sci. 2009 Jul;12(3):253-62.

John David and **Kristopher Irizarry** "Using the PubMatrix literature mining resource to accelerate student-centered learning in a veterinary PBL curriculum" Journal of Veterinary Medical Education, 2009 Summer;36(2):202-8.

Irizarry K, Merriman B, Bahamonde M, Wong M-L, Licinio J. The evolution of signaling complexity suggests a mechanism for reducing the genomic search space in human association studies. Molecular Psychiatry 2005 AOP doi:10.1038/sj.mp.4001576.

Wong M-L, O'Kirwan F, Hannestad JP, **Irizarry KJL**, Elashoff D, Licinio J. "St. John's wort and imipramine-induced gene expression profiles identify cellular functions relevant to antidepressant action and novel pharmacogenetic candidates for the phenotype of antidepressant treatment response". Molecular Psychiatry 2004; 9:237-251.

Licinio J, O'Kirwan F, **Irizarry K**, Merriman B, Thakur S, Jepson R, Lake S, Tantisira KG, Weiss ST, Wong M-L. "Association of a corticotropin-releasing hormone receptor 1 haplotype and antidepressant treatment response in Mexican Americans". Molecular Psychiatry 2004 AOP doi:10.1039/sj.mp.4001587

Irizarry, K., Hu, G., Wong, M-L., Licinio, J., Lee., CJ "Single Nucleotide Polymorphism Identification in Candidate Gene Systems of Obesity" The Pharmacogenomics Journal 1(3):193-203, 2001.

Lee, C. and **Irizarry, K.** "The GeneMine System for Genome Proteome Annotation and Collaborative Data Mining" IBM Systems Journal 40(2) 592-603 2001.

Irizarry, K., Kustanovich, V., Cheng, L., Brown, N., Nelson, S., Wong, W., Lee, C.J. "Genome Wide Analysis of Single Nucleotide Polymorphisms in Human Expressed Sequences" Nature Genetics 26: 233-236, 2000.

Salerno, J.C., Harris, D.E., **Irizarry, K.**, Patel, B., Morales, A.J., Smith, S.M.E., Jones, C., Weissman, B.A., Liu, Q., and Gross, S.S. "The autoinhibitory control element defines calcium regulated isoforms of nitric oxide synthase" Journal of Biological Chemistry 272 (47) :29769 -29777 Nov. 1997

Reid, Larry D., Hubbell, Christopher L., Glick, Stanley D., Boswell, Karen J., Chen, Alice M, Moran, Catherine M., Cramer, Christopher M., Mullen, Ursula D., Chambers, Michael D., Gonzales, Patricia M., **Irizarry, Kristopher L.**, and Amendola, Christopher A., "Initial Analysis of Naltriben, a Delta Opioid Antagonist, As a Putative Medicine for Treating Cocaine Abuse." Experimental and Clinical Psychopharmacology 4, 271-284, 1996.

NON-PEER REVIEWED PAPERS

Irizarry KJ, Licinio J. "An explanation for the placebo effect?" *Science* March 307 (5714) 2005.

Irizarry KJ, Galbraith SJ. "Significance of SNP combination patterns" Molecular Psychiatry 9(5):430 2004.

Irizarry KJ, Galbraith SJ. "Complex disorders reloaded: causality, action, reaction, cause and effect." Molecular Psychiatry, 9(5):431-2 2004.

Lee, CJ, **Irizarry, K.**, "Alternative Splicing in the Nervous System: An Emerging Source of Diversity and Regulation" Biological Psychiatry 54(8):771-6 2003.

BOOK CHAPTERS:

Kristopher J. L. Irizarry "Bioinformatics approaches for identifying allelic variants in candidate pathways underlying major depression and antidepressant treatment response" *Biology of Depression* Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim Germany 901-942 copyright 2005.

PATENTS

Licinio, Julio; Wong, Ma-Li; Irizarry, **Kristopher, J., L.**; Irizarry, Katherine, Misouras. "Compositions and methods for determining and predicting treatment responses for depression and anxiety" PCT/US2005/028790, Publication Date:16.02.2006 International Filing Date:12.08.2005

Summary of Points (Pt.1)

- Domesticated dogs were bred for specific morphological and anatomical traits
- The breed-associated anatomical traits are encoded by a very small number of genes (19,000 genes in dog genome, 6 control head shape)
- Tens of thousands of genes are responsible for wiring the mammalian brain and contributing to its function and the behavior of an organism

Summary of Points (Pt.2)

- Identifying anatomical features such as head shape, coat length, coat color, body size, musculature only indicate that the genetic signals encoding those traits are contained in a dog's genome
- There is no scientific basis for assuming that shared anatomical features among dogs correlates with shared brain organization or behavior – in fact there is very strong scientific, genetic and neuroscience evidence against this view

Summary of Points (Pt.3)

- Breeds were designed to conform to a physical breed standard. Subsequently, the stratification of dog breeds resulted in breed members sharing key anatomical / morphological traits.
- The genetic basis for the sharing of these anatomical traits is well described by researchers from MIT and Harvard and NIH who have systematically sequenced the dog genome and determined that roughly 50 genes are responsible for breed associated differences in appearance

Summary of Points (Pt.4)

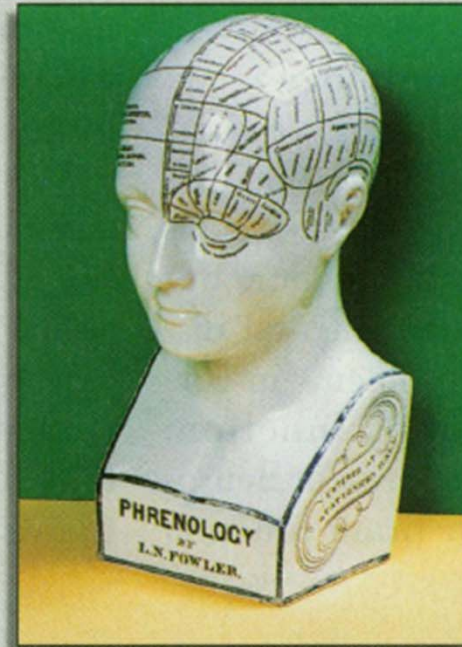
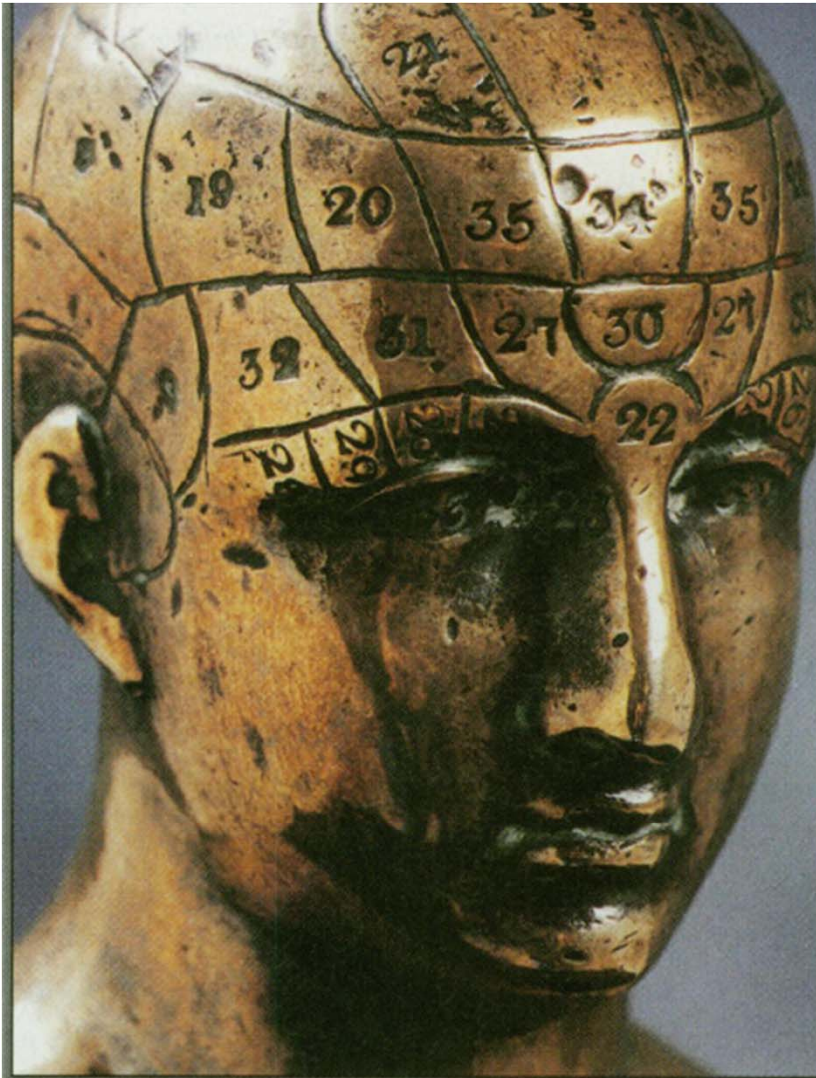
- Dogs visually identified as dangerous breeds are identified on the basis of specific anatomical traits that are encoded by a handful of genes
- The genes associated with morphological traits of dogs visually identified as dangerous dogs are not involved in the development, wiring, organization or function of the dog's brain
- Recent studies have identified over 17,000 genes within hundreds of anatomical regions of the mammalian brain. This complex organ and molecular system can not be inferred from tens of genes encoding head shape, snout length, body size and coat color/texture

Summary of Points (Pt.5)

- The accurate identification of breeds within mixed breed dogs is impossible because only 50 or so genes out of almost 20,000 genes in the dog genome control the external physical appearance of domestic dogs.
- $50 \text{ genes} / 20,000 \text{ genes} = 0.25\%$
- LESS THAN 1% OF THE DOG'S GENOME ENCODES IT'S BREED ASSOCIATED PHYSICAL TRAITS

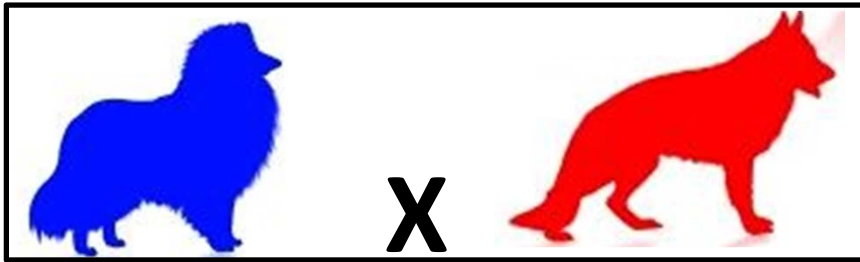
Summary of Points (Pt.6)

- The notion that one can infer dangerous neurological structures in a mammalian brain OR dangerous motivations on the basis of anatomical traits is not rational for three reasons:
 - 1. The genes encoding the anatomical traits do not encode the brain traits
 - 2. The presence of anatomical traits provides absolutely no inference about genes encoding behavioral traits
 - 3. Phrenology, the practice of inferring human personality traits from the shape of the skull was debunked at the turn of the 20th century and should not be the basis of 21st century laws

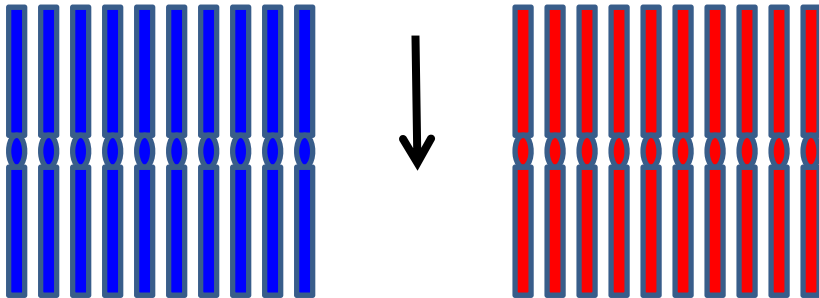


Earthenware phrenology head by L.N. Fowler: *The head stands 28 cm and bears the following inscription on the back: "For 30 years I have studied crania and living heads from all parts of the world, and have found in every instance that there is a perfect correspondence between the conformation of the healthy skull of an individual and his known characteristics. To make my observations available I have prepared a bust of superior form and marked the divisions of the organs in accordance with my researches and varied experience."*

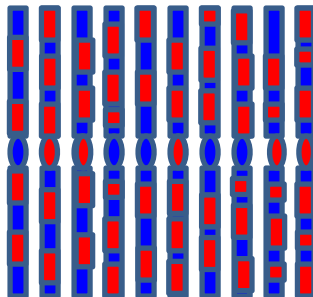
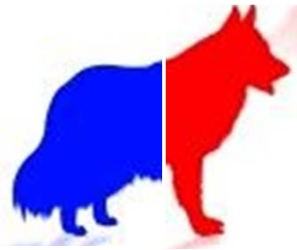
Phrenology was an attempt to infer personality traits from surface properties of the head



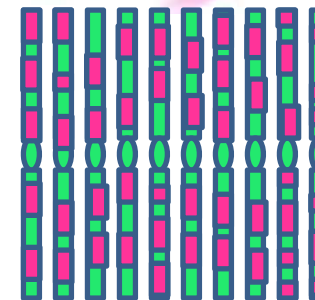
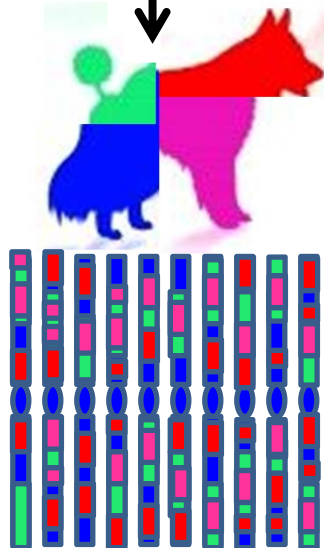
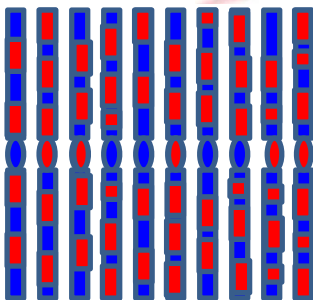
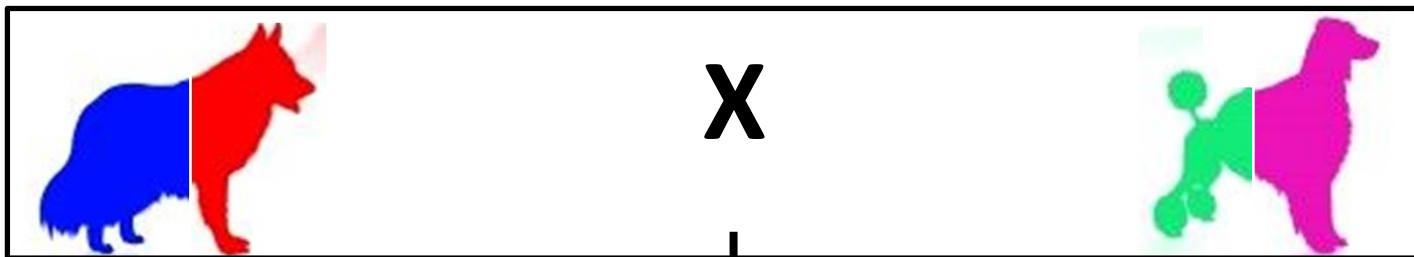
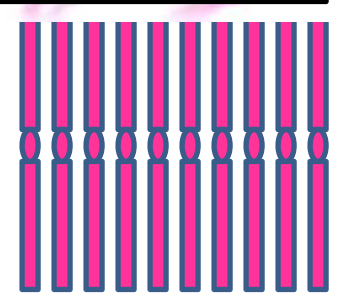
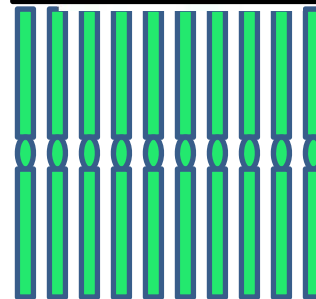
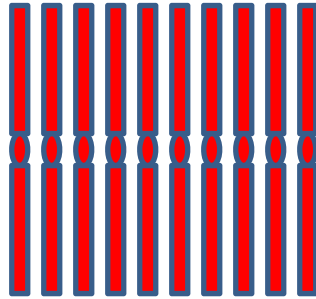
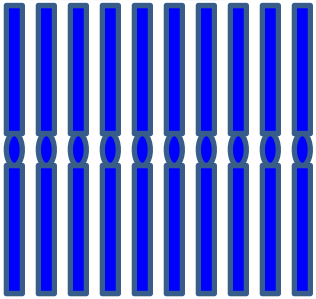
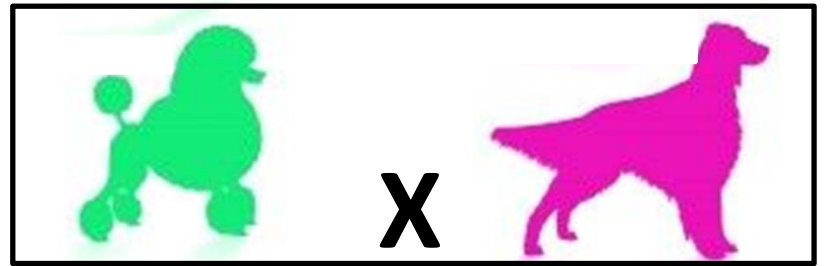
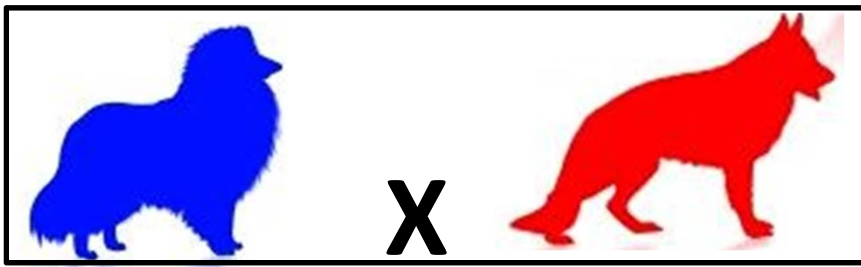
Offspring derive half of their DNA from each parent.



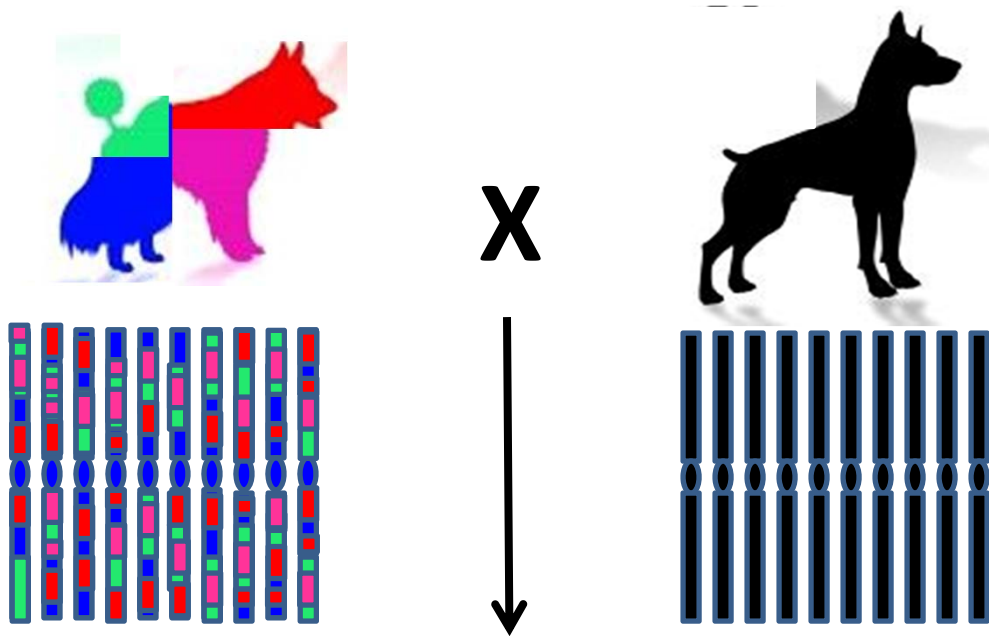
The reproductive cross of two different pure breeds will result in a dog that contains 50% of the DNA from each ancestral breed.



The offspring of this cross is NOT a member of either of the parental breeds as it lacks 50% of each parental breeds' DNA.



A dog that is only 25% of a specific breed lacks 75% of the genome from that breed. Such a dog is much more genetically similar to “dogs in general” than it is to one of its ancestral breeds.



All five puppies in the litter have the same mixed breed proportions but each puppy has a distinctly unique genome derived from ancestors

