Opportunities and challenges of genome editing in livestock for Latin America

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Livestock in LATAM

- “Although Latin America and the Caribbean account for only 13.5% of the world's population, they produce a little over 23% of beef and buffalo meat and 21.40% of poultry at global level. In the case of eggs and milk, the region contributes more than 10% and 11.2% by weight, respectively” (FAO)

Source: http://www.fao.org/americas/perspectivas/produccion-pecuaria/en/ - 23June17

Livestock in LATAM

- Brazil, Argentina and Mexico are among the largest milk producer countries

País/Ano3	2010 milhares de ton	2011 milhares de ton	2012 milhares de ton	2013 (*) milhares de ton	2014 (**) milhares de ton
União Europeia (***)	135.472	138.220	139.000	139.100	140.000
EUA	87.474	88.978	90.824	91.444	93.123
Índia	50.300	53.500	55.500	57.780	60.125
China	29.300	30.700	32.600	34.500	37.000
Brasil	**30.700**	**32.100**	**32.300**	**34.260**	**36.830**
Rússia	31.847	31.464	31.917	31.400	31.400
Nova Zelândia	17.173	18.965	20.567	19.678	20.569
Argentina	10.600	11.470	11.679	11.796	12.209
México	11.033	11.046	11.274	11.270	11.350
Ucrânia	10.977	10.804	11.080	11.160	11.220
Austrália	9.327	9.568	9.811	9.570	9.880
Canadá	8.350	8.400	8.614	8.535	8.450
Japão	7.721	7.474	7.631	7.560	7.580
Uruguai (****)	1.910	2.210	2.316	2.432	2.554
TOTAL	441.432	453.514	464.303	468.605	478.835

Fonte: USDA (United States Department of Agriculture) - Dairy: World Markets and Trade Dic 2013

(*) Dado preliminar

(**)Projetado

(***) Com base em referências

(****) Fonte: Estatísticas de DIEA 2013, MGAP.

Source: http://www.sindilat.com.br/index.php/noticias/163-producao-de-leite-do-rs-cresce-quase-o-dobro-da-do-brasil-nos-ultimos-dez-anos

Livestock in LATAM

- And beef production

World Beef Production: Ranking Of Countries			
World		59,001,000	
Rank	Country	2016	% Of World
1	United States	11,328,000	19.20%
2	Brazil	9,620,000	16.30%
3	European Union	7,680,000	13.02%
4	China	6,785,000	11.50%
5	India	4,300,000	7.29%
6	Argentina	2,680,000	4.54%
7	Australia	2,180,000	3.69%
8	Mexico	1,865,000	3.16%
9	Pakistan	1,775,000	3.01%
10	Russia	1,310,000	2.22%
11	Canada	1,065,000	1.81%
12	South Africa	885,000	1.50%
13	Colombia	855,000	1.45%
14	New Zealand	659,000	1.12%
15	Paraguay	590,000	1.00%
16	Uruguay	575,000	0.97%
17	Japan	475,000	0.81%
18	Kazakhstan	425,000	0.72%
19	Philippines	415,000	0.70%
20	Ukraine	370,000	0.63%
21	Egypt	360,000	0.61%
22	South Korea	308,000	0.52%
23	Belarus	290,000	0.49%

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Source: http://beef2live.com/story-world-beef-production-ranking-countries-0-106885

Livestock in LATAM

- But also in poultry production

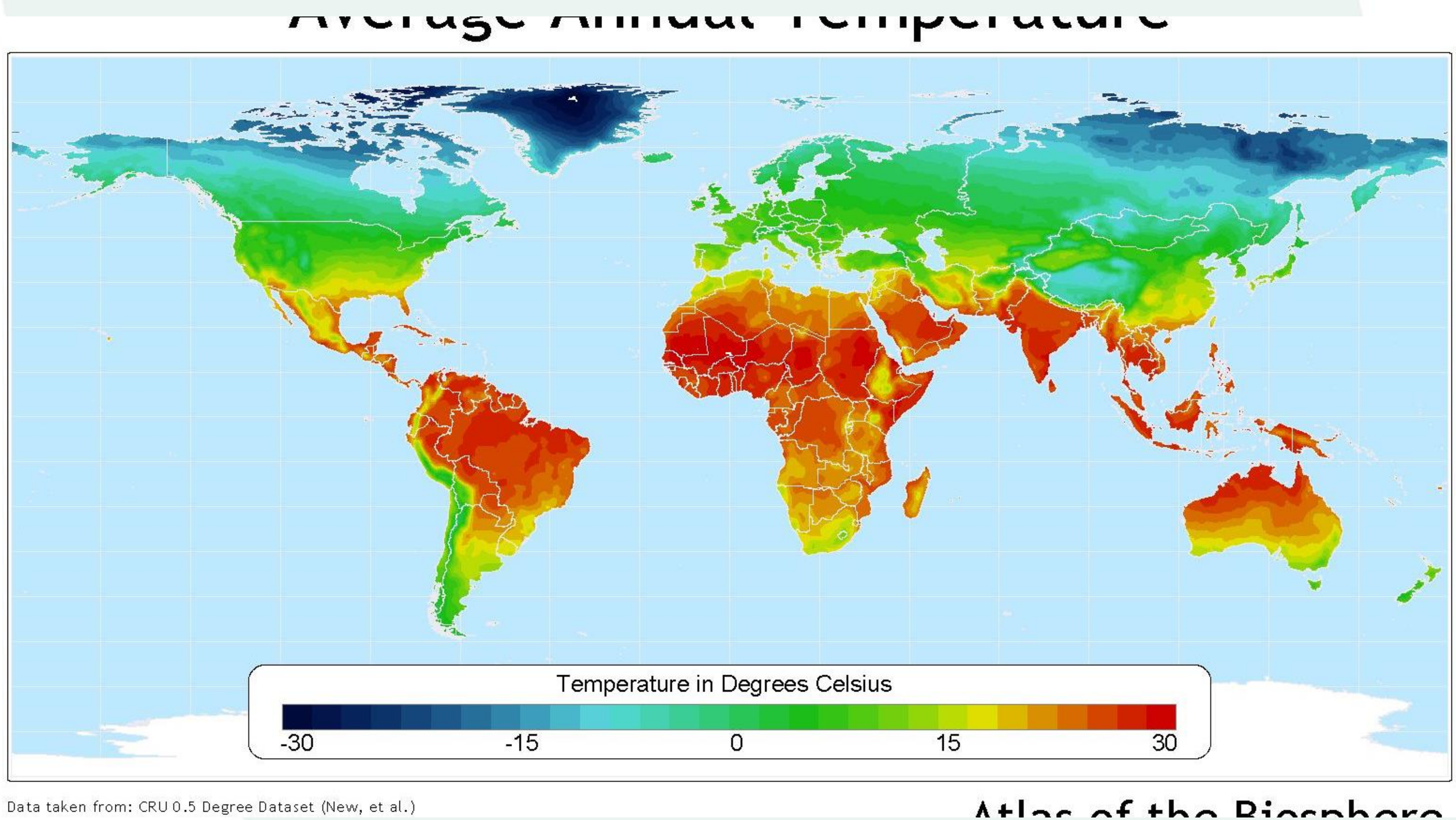
Broiler Meat (Poultry) Production by Country in 1000 MT

Rank	Country	Production (1000 MT)
1	United States	17,752.00
2	Brazil	13,115.00
3	China	13,000.00
4	EU-27	10,300.00
5	India	3,900.00
6	Russian Federation	3,400.00
7	Mexico	3,150.00
8	Argentina	2,160.00
9	Turkey	1,800.00
10	Thailand	1,640.00
11	Indonesia	1,625.00
12	Malaysia	1,460.00
13	South Africa	1,435.00
14	Colombia	1,390.00
15	Japan	1,360.00
16	Canada	1,100.00
17	Australia	1,080.00
18	Ukraine	1,010.00
19	Philippines	910.00
20	Viet Nam	810.00
21	Korea, Republic Of	753.00
22	Saudi Arabia	710.00
23	Venezuela	680.00
24	Chile	595.00
25	Taiwan, Province Of China	475.00
26	Belarus	390.00
27	Jordan	235.00
28	Guatemala	196.00
29	Kazakhstan	180.00
30	Yemen	135.00
31	Azerbaijan	112.00
32	Iraq	110.00
33	Singapore	98.00
34	Ghana	60.00
35	Kuwait	47.00

Source: http://canadiansmallflockers.blogspot.com/2015/04/chicken-exporters-for-world.html

Geographic position LATAM

Average annual temperature



Sorce: https://nelson.wisc.edu/sage/data-and-models/atlas/maps/avganntemp/atl_avganntemp.jpg

Important issues for livestock production in LATAM

- Heat stress
  - Reduces production and fertility
- Tropical diseases and parasite infestations
  - Ticks and ticks born-diseases; horn flies, foot-and-mouth disease, etc.
- Low digestibility of tropical forages/ grasses
  - Tropical forages grow at fast rate but also lose quality very fast

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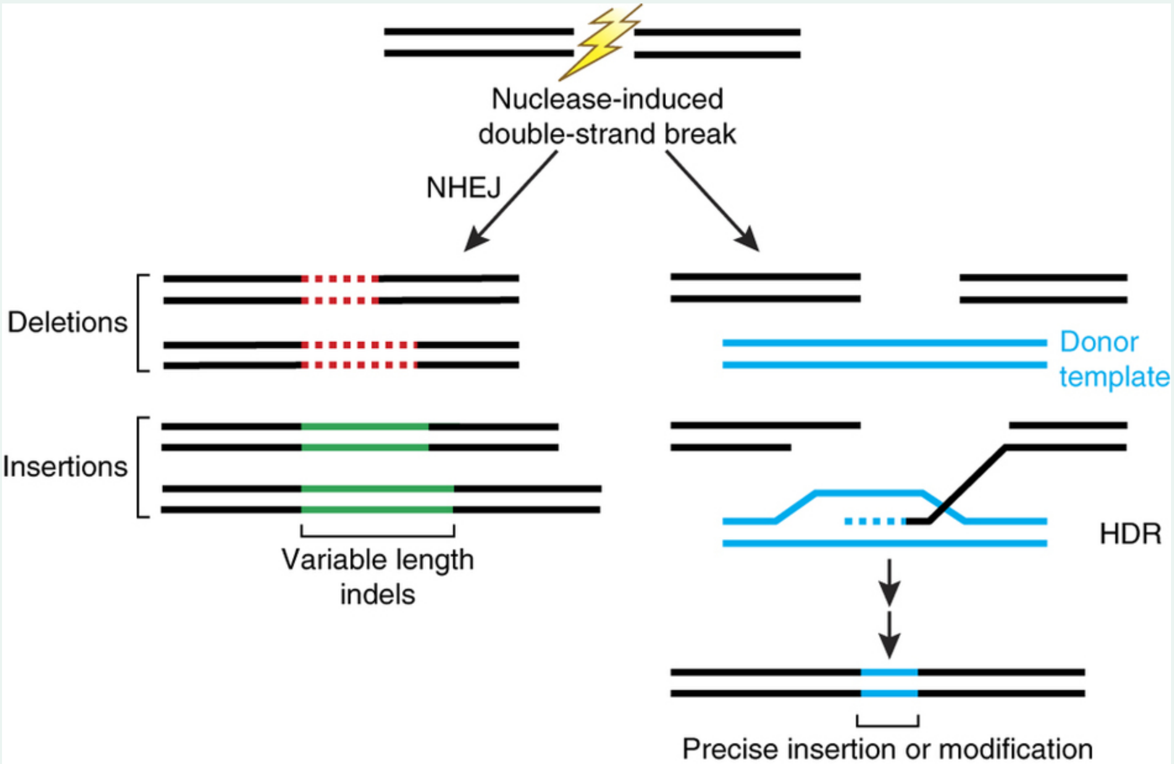
Which opportunities may we have with genome editing for LATAM livestock?



nature
biotechnology

CRISPR-Cas systems for editing, regulating and targeting genomes

Jeffry D Sander[1,2] & J Keith Joung[1,2]

Image: http://m.milkpoint.com.br/radar-tecnico/bemestar-e-comportamento-animal/vantagens-do-manejo-do-estresse-calorico-em-gado-leiteiro-86072n.aspx

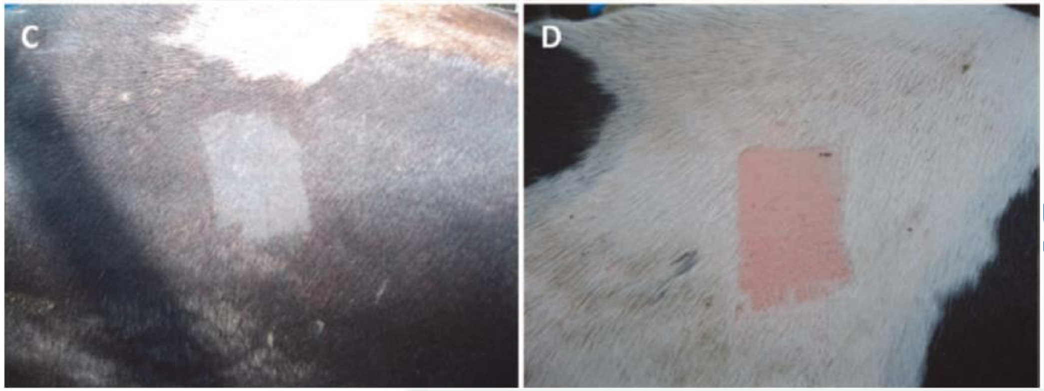
Increase the thermotolerance

- Introgression of genes or mutations associated to heat tolerance
  - Ex. Slick hair locus derived from Senepol (Bos taurus) cattle may confer thermotolerance
    - short hair length
      - Holstein cows with short hair - more tolerant to heat stress

Evidence of a major gene influencing hair length and heat tolerance in *Bos taurus* cattle[1,2,3]

T. A. Olson*[4], C. Lucena†, C. C. Chase, Jr.‡, and A. C. Hammond‡[5]

*University of Florida, Gainesville 32611; ‡USDA, ARS, Subtropical Agricultural Research Station, Brooksville, FL 34601; and †Universidad Centrooccidental "Lisandro Alvarado," Barquisimeto, Venezuela



J. Dairy Sci. 97:5508–5520
http://dx.doi.org/10.3168/jds.2014-8087

The *SLICK* hair locus derived from Senepol cattle confers thermotolerance to intensively managed lactating Holstein cows

S. Dikmen,* F. A. Khan,†[1] H. J. Huson,‡[2] T. S. Sonstegard,‡ J. I. Moss,† G. E. Dahl,† and P. J. Hansen†[3]
*University of Uludag, Faculty of Veterinary Medicine, Department of Animal Science, Bursa 16059, Turkey
†University of Florida, Department of Animal Sciences, Gainesville 32611-0910
‡USDA, Agricultural Research Service, Animal Genomics and Improvement Laboratory, Beltsville, MD 20705-2350

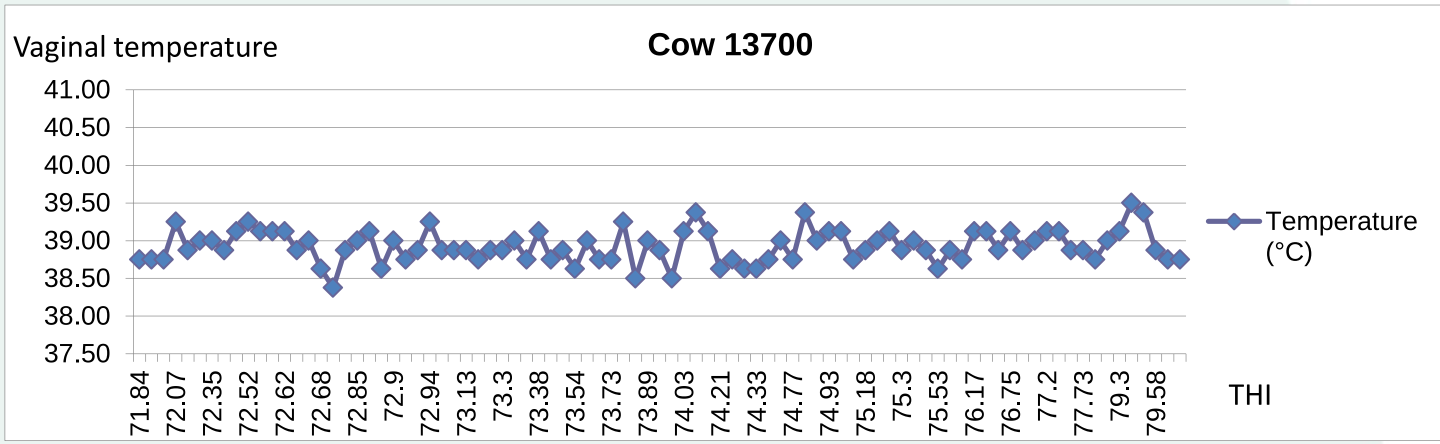
Image: LS Camargo

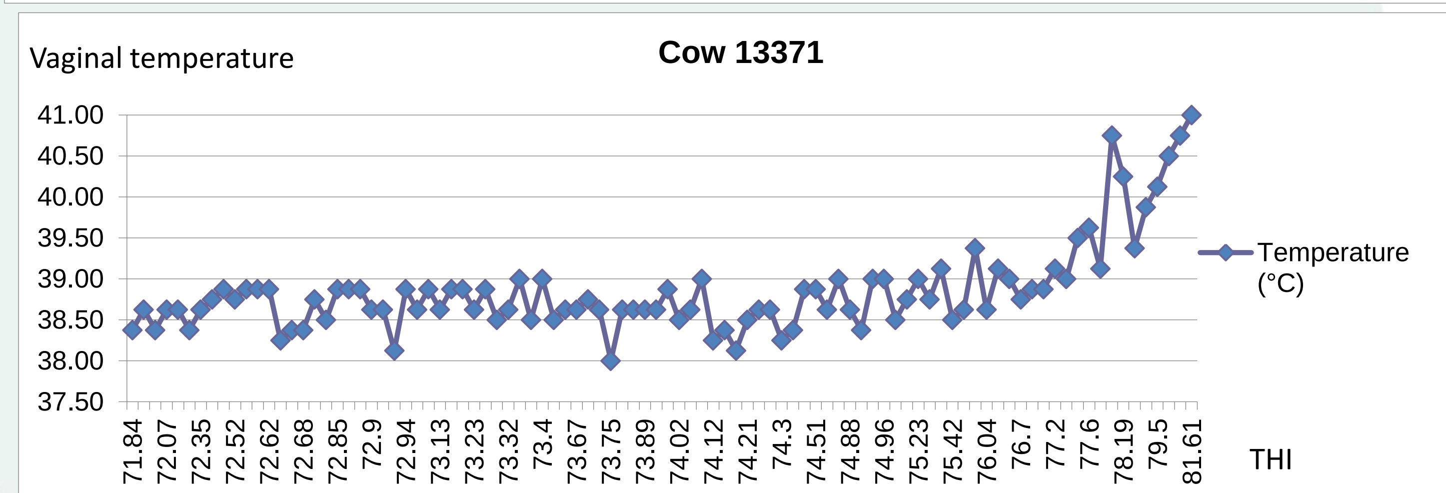
Cattle thermotolerance

- Girolando (Hostein x Gir crossbred) cows with different ability to deal with high temperature and humidity index (THI)

- Search for polymorphism associated to thermotolerance- GWA study

- discover of new genes or mutations





Control of ticks population

- Ticks
  - High infestation reduces production
    - Uses of insecticides – milk withholding period
      - Resistance to insecticides

  - diseases vector (babesiosis and anaplasmosis)

Image: http://www.cnpgl.embrapa.br/sistemaproducao/410211-controle-de-carrapatos-–-rhipicephalus-boophilus-microplus

Control of ticks population

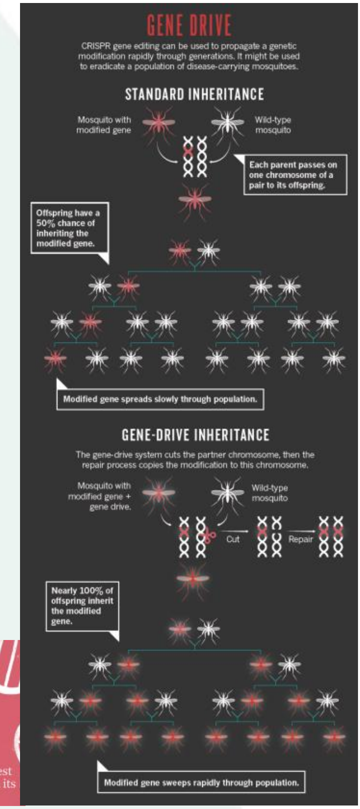
- CRISPR/Cas9 and gene drive
  - Ex: mosquito Anopheles -Malaria vector
    - Three genes that confers sterility

LETTERS

nature biotechnology

A CRISPR-Cas9 gene drive system targeting female reproduction in the malaria mosquito vector *Anopheles gambiae*

Andrew Hammond[1], Roberto Galizi[1], Kyros Kyrou[1], Alekos Simoni[1], Carla Sinisclachi[2], Dimitris Katsanos[1], Matthew Gribble[1], Dean Baker[3], Eric Marois[4], Steven Russell[3], Austin Burt[1], Nikolai Windbichler[1], Andrea Crisanti[1] & Tony Nolan[1]



- Repairing mutations that cause insecticides resistance
  - Example: two mutation in a putative receptor in ticks resistant to Amitraz – a very common insecticide

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ELSEVIER
Available online at www.sciencedirect.com
ScienceDirect
Veterinary Parasitology 148 (2007) 379–383
veterinary parasitology
www.elsevier.com/locate/vetpar

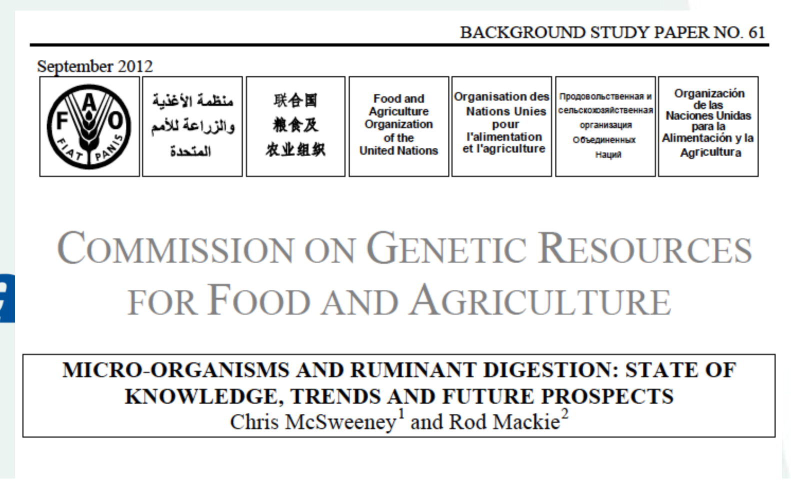
Rapid communication

Mutations in a putative octopamine receptor gene in amitraz-resistant cattle ticks

Andrew C. Chen[a,*], Haiqi He[b], Ronald B. Davey[c]

Increase the rumen digestibility

- Low digestibility of tropical forages – due to high content of hemi-cellulose and/or lignin
  - Can not be digested by rumen microbiome - lack of enzymes
  - Modification of rumen microbiome to express fibrolytics or ligninolytic enzymes:
    - Xilanases (hemi-cellulose), laccases (lignin), etc
  - Contributes to increase feed efficiency


BACKGROUND STUDY PAPER NO. 61

September 2012

FAO FIAT PANIS	منظمة الأغذية والزراعة للأمم المتحدة	联合国粮食及农业组织	Food and Agriculture Organization of the United Nations	Organisation des Nations Unies pour l'alimentation et l'agriculture	Продовольственная и сельскохозяйственная организация Объединенных Наций	Organización de las Naciones Unidas para la Alimentación y la Agricultura

COMMISSION ON GENETIC RESOURCES FOR FOOD AND AGRICULTURE

MICRO-ORGANISMS AND RUMINANT DIGESTION: STATE OF KNOWLEDGE, TRENDS AND FUTURE PROSPECTS

Chris McSweeney[1] and Rod Mackie[2]

Technical challenges

- Off-targets
  - Recent concerns about *in vivo* off-targets and theirs effects on animals

NATURE METHODS | CORRESPONDENCE

Unexpected mutations after CRISPR–Cas9 editing *in vivo*

Kellie A Schaefer, Wen-Hsuan Wu, Diana F Colgan, Stephen H Tsang, Alexander G Bassuk & Vinit B Mahajan

Nature Methods 14, 547–548 (2017) doi:10.1038/nmeth.4293
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To the Editor:

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Author Manuscript
Dev Biol. Author manuscript; available in PMC 2014 September 18.
Published in final edited form as:
Dev Biol. 2014 September 1; 393(1): 3–9. doi:10.1016/j.ydbio.2014.06.017.

Somatic mosaicism and allele complexity induced by CRISPR/Cas9 RNA injections in mouse zygotes

Shuo-Ting Yen[a,b], Min Zhang[c], Jian Min Deng[b], Shireen J. Usman[b], Chad N. Smith[d], Jan Parker-Thornburg[d], Paul G. Swinton[e], James F. Martin[a,c,e], and Richard R. Behringer[a,b,*]

- Gene drive and species extinction
  - Uncontrolled transmission of the gene

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Evolution of Resistance Against CRISPR/Cas9 Gene Drive

Robert L. Unckless, Andrew G. Clark and Philipp W. Messer

GENETICS February 1, 2017 vol. 205 no. 2 827-841; https://doi.org/10.1534/genetics.116.197285

Science & Society
OPEN ACCESS
EMBO reports

Agricultural pest control with CRISPR-based gene drive: time for public debate

Should we use gene drive for pest control?

Virginie Courtier-Orgogozo[1], Baptiste Morizot[2] & Christophe Boëte[3]

Technical challenge

- Genome edited animal production in large scale
  - SNCT (animal cloning) very low efficiency,
  - Cytoplasm injection – required to cross the zona pelucida
    - Oocyte or zygote need to be micromanipulated individually

  - Need for less labor and efficient methods to transfect embryos

SCIENTIFIC REPORTS

OPEN

Efficient delivery of DNA into bovine preimplantation embryos by multiwall carbon nanotubes

Received: 12 May 2016
Accepted: 24 August 2016
Published: 19 September 2016

Michele Munk[1], Luiz O. Ladeira[2], Bruno C. Carvalho[3], Luiz S. A. Camargo[3], Nádia R. B. Raposo[1,4], Raquel V. Serapião[3], Carolina C. R. Quintão[3], Saulo R. Silva[3], Jaqueline S. Soares[5], Ado Jorio[2] & Humberto M. Brandão[3]

Technical challenge

- Genomic and phenotypic studies:
  - in tropical enviroment
  - need of basic information to identify the correct targets genes, mutations, etc
    - Are the products of those genes involved in different metabolic pathways?

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Concerns

- Public conception that animal genetic engineering is bad or demoniac
  - Even mutations already present in the specie
  - Public acceptance
  - International trade

Image: https://br.pinterest.com/kitway1/dragon/

Acknowledges

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Thank you
Muito obrigado