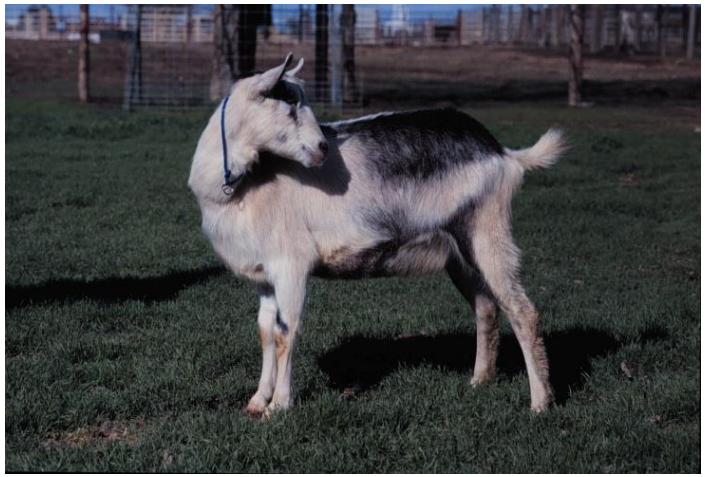
Transgenic Animals for Agriculture: Current status and prospects



James D. Murray

Department of Animal Science

Department of Population Health and Reproduction

University of California, Davis CA 95616 USA

The imperative is simple: Given the increasing world population

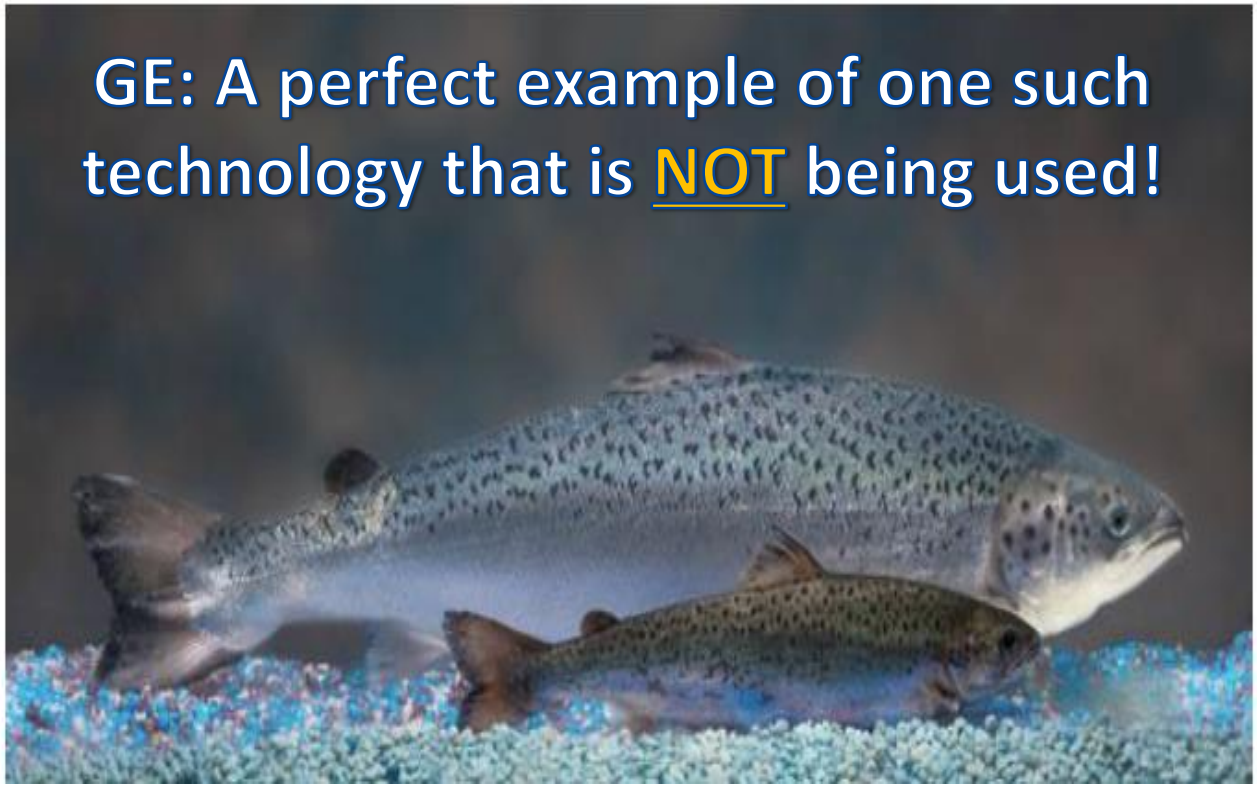
- **Animal production must be increased using less land, less water, and in a sustainable manner**

- **We need to use all tools available:**

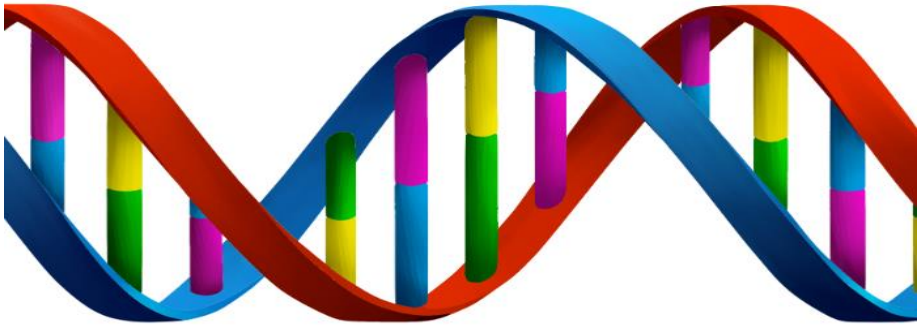
  nutrition
  management
  vaccines
  ART (including cloning)
  selective breeding
  genetic engineering
  gene editing

AquaBounty TECHNOLOGIES

AquAdvantage Salmon



Keep in mind - in the USA DNA is the regulated article



Currently for animals the insertion of DNA is the trigger for regulation

FDA defines transgene DNA as a New Animal Drug

Transgene inherited through normal breeding considered drug residue

BIOTECHNOLOGY IS NOT THE BOTTLENECK

- We can now, and indeed have, produced GE animals suitable for food
- The applications and potential benefits are real

As I see it:

Compared to plants, GE livestock (but not necessarily fish), pose essentially zero threat to the environment and biodiversity.

Experience with GE plants and animals indicate they pose little to no food safety risk to people.

GE crops widely embraced and their products have been consumed in billions of meals.

As of today

November 2015 - first GE animal product approved for food anywhere in the world – the AquAdvantage Salmon …..

But you still cannot buy it anywhere in the world

Since 2008, majority of lines of TG livestock for food produced in China, but none have been approved!

Genetically engineered animals are available

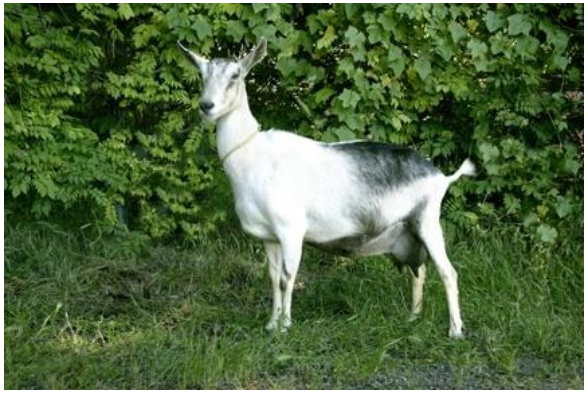
Deliver the intended benefits

No identified negative effects

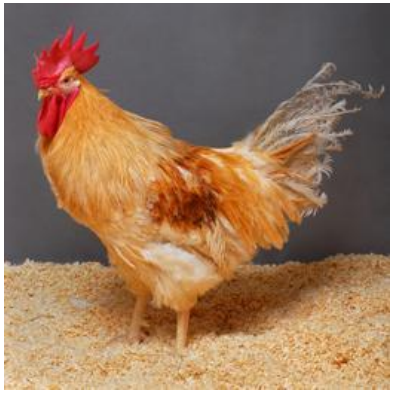
Some GE animals available today

the enviro-pig™

bα-lactalbumin pigs



h-lysozyme goats



flu resistant chickens

Transgenic animals produced and characterized for use in agriculture

			References
Species	Transgene*	Production	Characterization
Pig	ba-LA/ba-LA	Bleck et al., 1998	Wheeler et al., 2001; Noble et al., 2002; Marshall et al., 2006
	mPSP/APPA	Golovan et al., 2001	Forsberg et al., 2003, 2013
	ba-LA/hIGF-I	Monaco et al., 2005	Hartke et al., 2005
Cattle	bCsn/hLF	van Berkel et al., 2002	Thomassen et al., 2005; Simojoki et al., 2010; Cooper et al., 2012, 2014
Goat	bαS_1Csn/hLz	Maga et al., 2003	Maga et al., 2006a, b, c, 2012; Scharfen et al., 2007; Brundige et al. 2008, 2010; Jackson et al., 2010, Cooper et al., 2011, 2013, 2014a, b; Carvalho et al., 2012; Clark et al., 2014, McInnis et al., 2015; Garas et al., 2016

***Transgenes: ba-LA/ba-LA-bovine α-lactalbumin, mPSP/APPA-mouse parotid secretory protein/*E. coli* phytase, ba-LA/hIGF-1- bovine α-lactalbumin/ human insulin like growth factor-1, bCsn/hLF-bovine casein/human lactoferrin, bCsn/hLz-bovine αS_1casein/human lysozyme.**

Presence of TG DNA and protein in food product

	Meat	Meat	Milk	Milk
	TG-DNA	TG-Protein	TG-DNA	TG-Protein
b-Lactalbumin-pig	yes	no	yes	yes
h-IGF-1 pig	yes	no	yes	yes
b-Csn/h-lactoferrin	yes	no	yes	yes
EnivroPig (E. coli phytase)	yes	no	yes	no
H-Lysozyme-goat	yes	no	yes	Yes
AquAdvantage salmon (csGH)	yes	yes	N.A.	N.A.

All of these proteins, have been, and are now consumed regularly – *i.e. when not GE are GRAS*

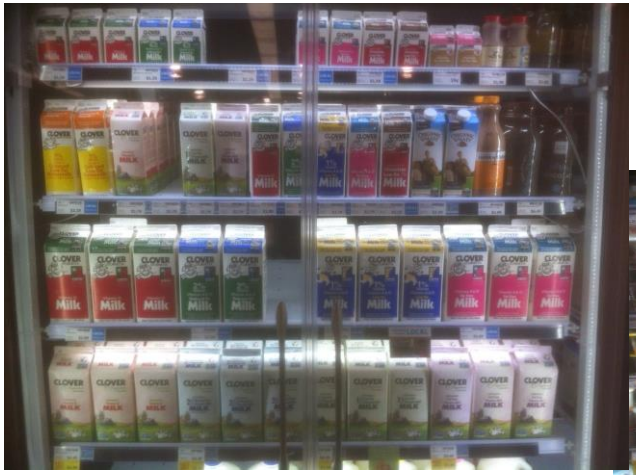
bovine alpha-lactalbumin pigs

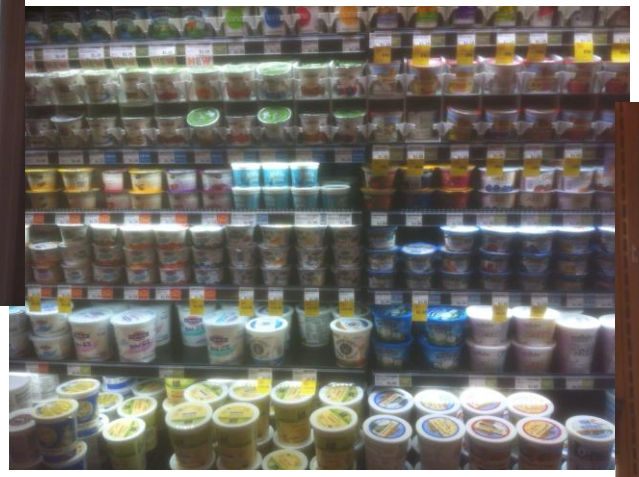
- Express bovine α-lactalbumin only in lactating mammary gland
- Sows produce more milk
- Baby pigs grow faster, heavier at weaning = increased sustainability

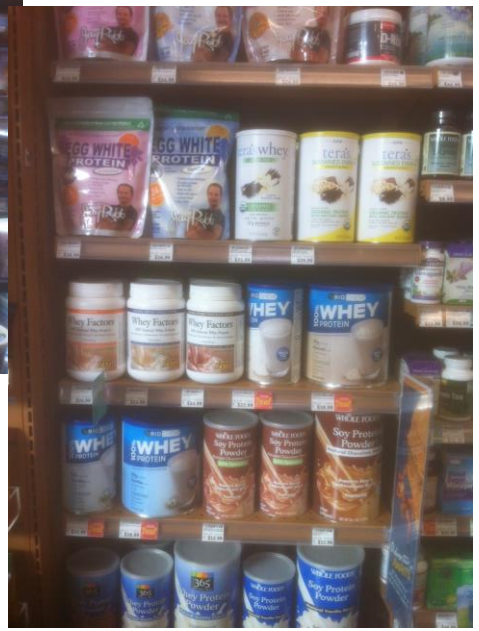
- Wean more pigs = improved animal welfare

Regulatory paradigm should reflect potential hazard and risk of harm

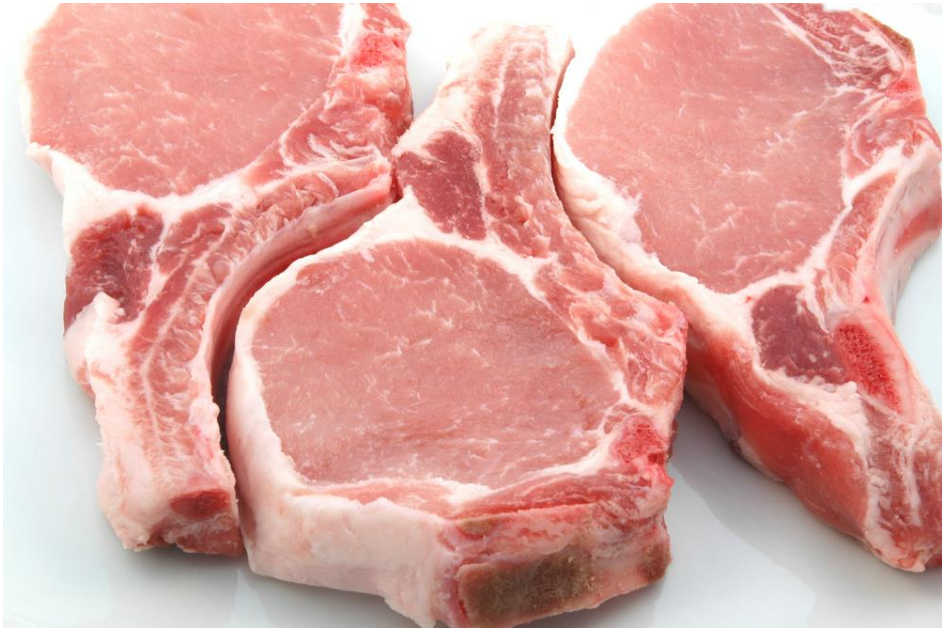
This we know: bovine lactalbumin is commonly consumed in:







Furthermore - meat from these animals does not contain alpha-lactalbumin –

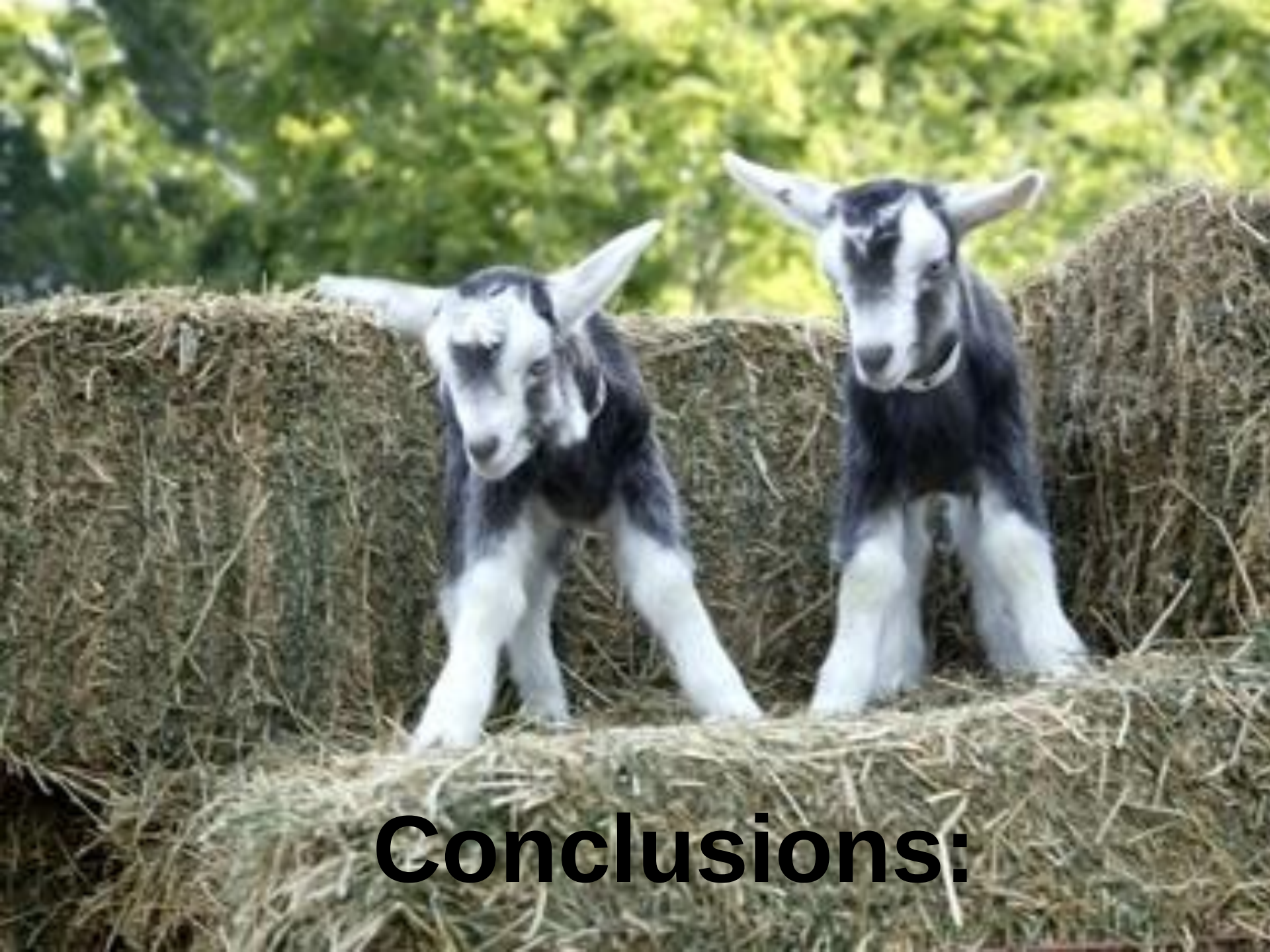


only transgene DNA

and DNA is Generally Recognized As Safe to eat

Other GE animals produced for agriculture since 1990

Species	Transgene*	Reference
Pig	maP2/FAD2	Saeki et al., 2004
	CAG/hfat-1	Lai et al., 2006; Pan et al., 2010
	bCsn/hLz	Tong et al., 2011
	U6-RNA /PRRSV^{siRNA}	Li et al., 2014
Cattle	cASK/hER	Hill, 1992; Massey, 1990
	bCsn/hLF	Krimpenfort et al., 1991
	MSV/cc-ski	Bowen et al., 1994
	bbCsn/bbCsn & bk-Csn	Brophy et al., 2003
	KO PrP^{BSE}	Richt et al., 2007
	hLA/hLA	Wang et al., 2008
	hLF/hLF	Yang et al., 2008
	bCsn/hLz	Yang et al., 2011
	?/fat-1	Guo et al., 2011
	EF1a/anti-GDF8 shRNA	Tessanne et al., 2012
	mMCKE-cbA/mfat-1	Wu et al., 2012
	mWAP-BLG-miRNA	Jabed et al., 2012
	bMSR1-Ipr1	Wang et al., 2015
Goat	bLG/SCD	Reh et al., 2004
	oCsn/hGH	Lee et al., 2006
	oCsn/hLF	Zhang et al., 2008
Sheep	RSV/CE, CK,	Rogers, 1990
	oMT/CE, CK	Ward and Nancarrow, 1991
	mKER/oIGF-I	Damak et al., 1996a
	U6-RNA/MSTN^{shRNA}	Hu et al., 2013



Conclusions:

Prospects for the use of transgenic animals in agriculture

1) Short term prospects seem unlikely

2) World-wide “Long” Regulatory timeframe hampers innovation and industry investment
   a. regulatory issues are political

3) Process vs product-based regulation

4) Activist opposition in the absence of scientific or clinical data showing problems