

Can single administration of a high dose GnRH agonist persistently suppress the canid reproductive axis? The coyote (*Canis latrans*) as a model



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UNIVERSITY OF WYOMING



### Deslorelin (Suprelorin®)



Long Term / Permanent Contraception

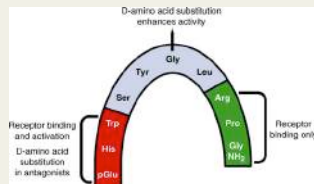
### Gonadotropin Releasing Hormone (GnRH) Analogs

Synthetic decapeptide (3,000)

Domestic cats and dogs

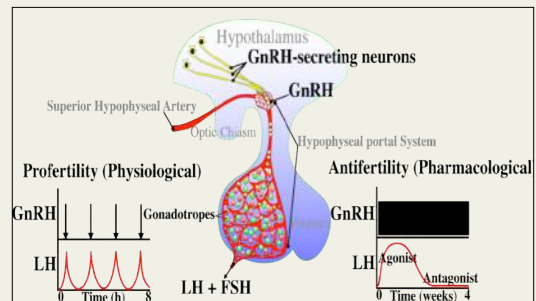
Exotic Species

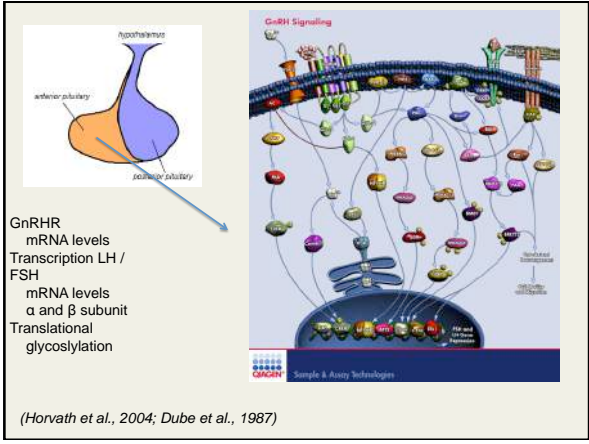
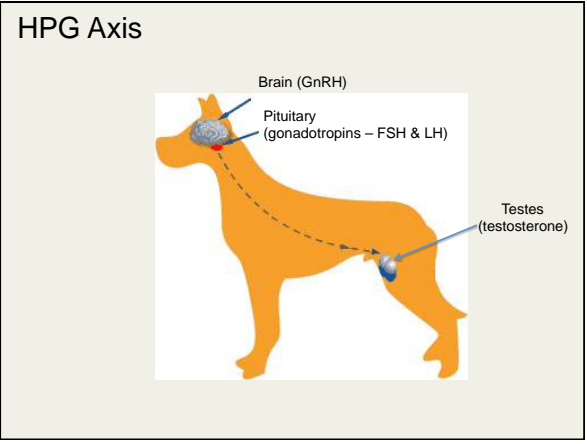
Safe and reversible (?)  
 effective (?)  
 males vs. females (?)



(Junaidi et al., 2001; Trigg et al., 2001; Junadi et al., 2009; Bertschinger et al., 2001, 2002; Millar 2005)

### (GnRH) Agonist



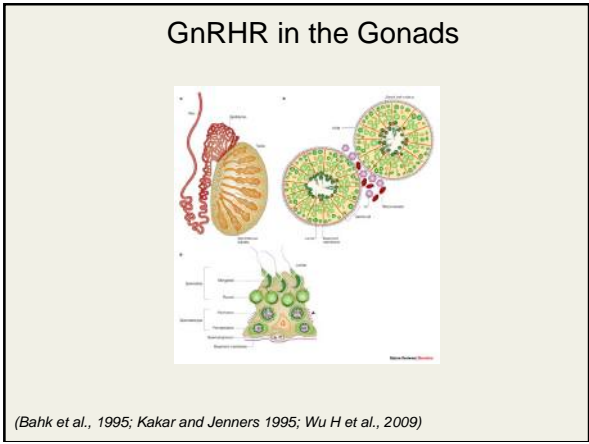


### Pituitary and Gonads

GnRH agonist and GnRH immunocontraception

GnRH agonist and GnRH antagonist

(Lunn et al., 1989; Herbert et al., 2004; Snape et al., 2012)





## Reversibility and Long Term

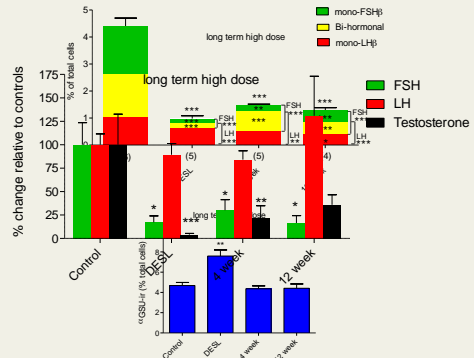
Table 1. Clinical details and hormonal baseline values (all patients with extracapsular prostatic cancer)

Case No.	Age years	Treatment months	LH IU/L	FHS IU/L	PRL µg/l	T nmol/l	
1	77	28	A	19.0	7.5	13.5	15.3
			B	11.3	7.8	5.0	0.6
			C	8.8	7.9	2.4	0.7
2	72	31	A	19.0	28.0	19.0	17.4
			B	12.6	5.5	13.3	1.1
			C	12.6	5.7	12.2	0.9
3	73	30	A	35.0	30.0	16.0	16.7
			B	12.6	13.5	1.6	0.4
			C	9.0	12.5	1.1	0.2
4	83	30	A	24.0	10.3	15.4	11.1
			B	7.7	4.1	2.2	0.6
			C	12.5	5.1	8.4	0.7
5	66	28	A	16.0	19.0	6.2	25.0
			B	10.8	10.6	6.5	1.6
			C	11.9	10.6	6.9	1.5
6	64	31	A	13.0	14.0	7.2	15.9
			B	6.8	6.6	2.8	0.3
			C	6.6	6.7	3.5	0.2
7	65	32	A	20.0	19.0	9.2	27.8
			B	6.4	12.1	2.6	0.8
			C	17.9	13.8	2.9	0.6

A = Pre-treatment values, B = values recorded at the end of treatment, C = values recorded 40 days after the end of treatment.

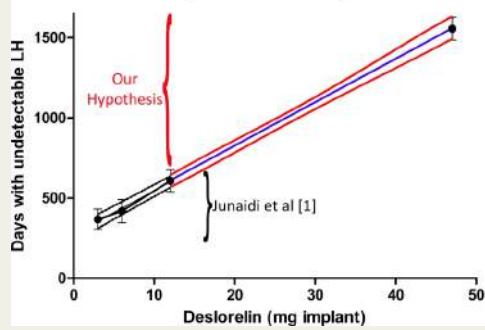
(Rolandi et al., 1988)

## High Dose Deslorelin in the Rat



(Edwards et al., in preparation)

## Effect of Deslorelin in the dog with hypothetical extrapolation for 47mg dose



(Junaidi et al., 2009)

## A Unique Collaboration: Coyote Model




Photo: Stan Gehrt

THE SACRAMENTO BEE  sacbee.com

May 29, 2012




Wildlife Services removes 65,000-100,000 coyotes annually




**Coyote contraception a potential alternative to curb population**

A good .223 curbs the population and is a lot more fun.

The coyotes aren't breeding the sheep, calves, deer & antelope. They are mutilating and eating and sometimes not even killing them. This really sounds like a good use of tax dollars??????

It's to bad that Macgregor's mother didn't use these contraceptives years ago. It would have solved one problem

Cabergoline




(DeLiberto et al., 2002)

**Single Treatment of a Sustained Release GnRH (deslorelin) Agonist May Chemically Neuter Coyotes**


1. Relationship between GnRH agonist dose on duration of suppression
2. Determine cytological pituitary and testicular changes
3. Establish high-dose GnRH agonist effect on pathophysiology

### Methods - Male Coyotes

Group 1 ( $n=3$ ) adults  
**47 mg deslorelin (9.4 mg)**  
 SQ on April 2011



Group 2 ( $n=5$ ) pre-pubertal  
**47 mg deslorelin (4.7 mg)**  
 SQ on January 2012




### Relationship Between GnRH Agonist Dose on Duration of Suppression



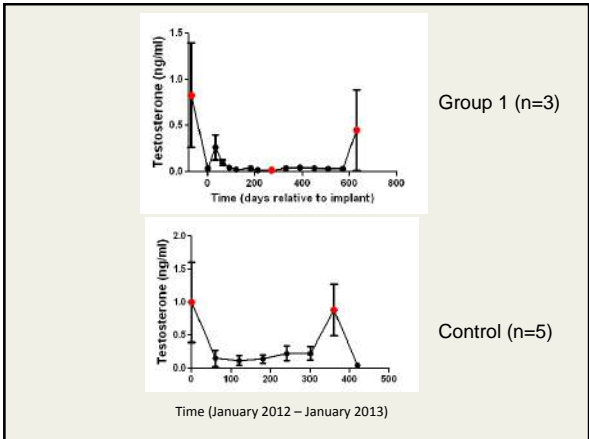
Reproductive Hormones

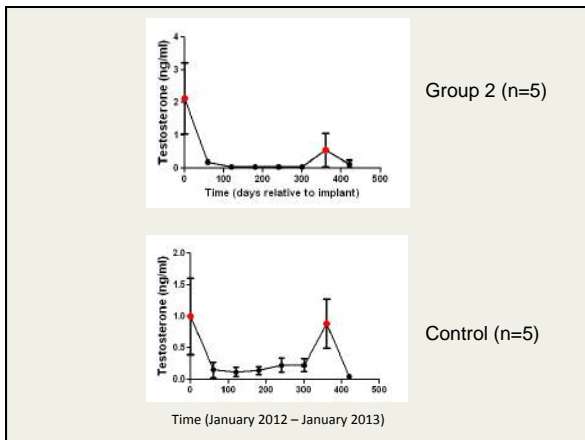


Sperm Concentration




Testes Volume

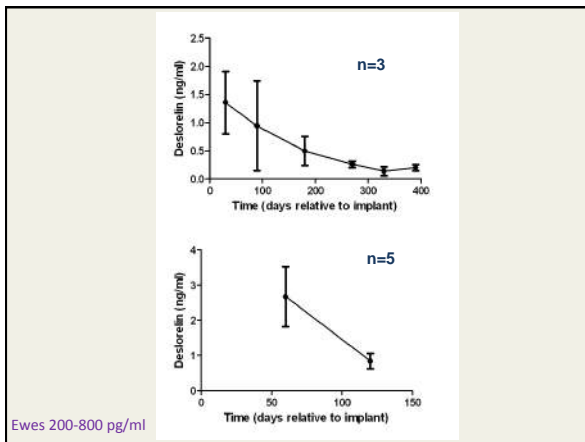




### Sperm (January 2013)



- n=2 (control)  
Testes Volume: 7.35 ml  
Sperm Concentration: 208 x 10<sup>6</sup>  
Testosterone: 1.431 ng/ml
- n=2 (pre-pubertal suppressed)  
Testes Volume: Below detection (skin)  
Sperm Concentration: 0  
Testosterone: 0.023 ng/ml
- n=2 (pre-puberty reversed)  
Testes Volume: 5.7 ml  
Sperm Concentration: 319 x 10<sup>6</sup>  
Testosterone: 0.069 ng/ml




### The Coyote Pituitary – Mechanisms



Fluorescence microscopy images showing:

- FSH $\beta$  (green)
- LH $\beta$  (red)
- Colocalized (yellow/green)

### Establish High-Dose GnRH Agonist Effect on Pathophysiology





Muscle mass, fat composition and bone mineral density

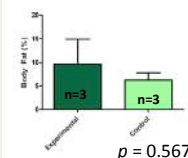



Metabolic Syndrome in **aged men** with prostate cancer (adiposity)


### M06073 Porky Pig

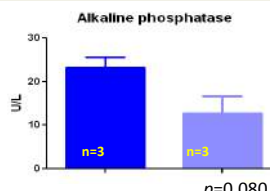
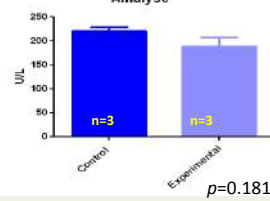
Region	Tissue (%Fat)	Centile	T.Mass (kg)	Fat (g)	Lean (g)	BMC (g)
Legs	12.7	-	-	691	4,740	97.8
Trunk	4.1	-	-	165	3,913	103.6
Total	9.3	-	12.63	1,138	11,136	355.5



$p = 0.567$




Blood Chemistry (17)  
Lipid Profiles (HDL/ LDL/Trig/Chol)

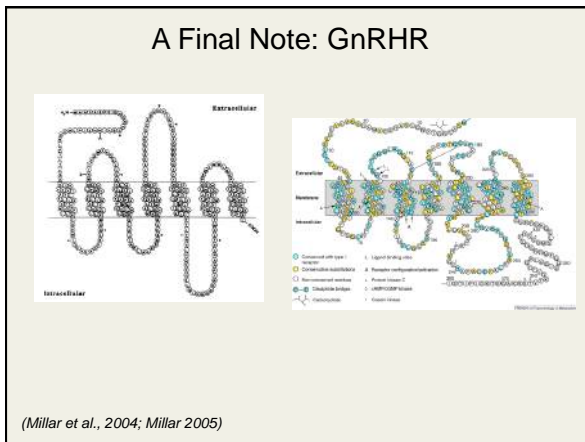
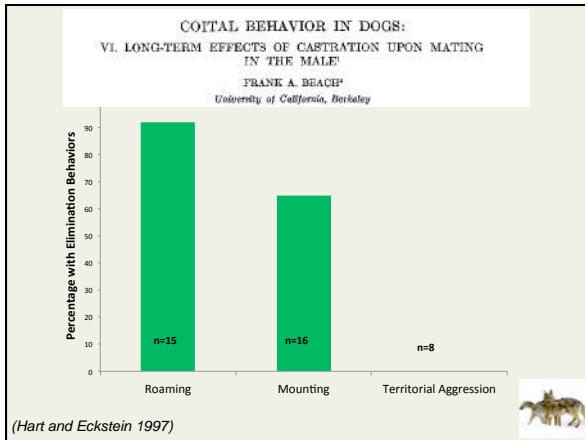



### Future Directions





GnRH Agonists (*Suprelorin*®) and GnRH Immunocontraception (*GonaCon*™)



### Acknowledgements:

**Funding / Collaboration / Support**

- Wyoming ADMB
- AZA Wildlife Contraception Center
- The Contraception Advisory Group
- USDA/APHIS/WS/NWRC Logan Field Station
- USDA/APHIS/WS Wyoming State Office
- AES LREC Beef Unit
- UW Research Office
- Colleagues in the Skinner Lab

**Graduate Committee**

- Donal Skinner, PhD (University of Wyoming)
- Cheryl Asa, PhD (St Louis Zoo)
- Liz Flaherty, PhD (University of Wyoming)
- Bill Murdoch, PhD (University of Wyoming)
- Brian Cherrington, PhD (University of Wyoming)
- Derek Smith, PhD (University of Wyoming)










Thank you



Questions?