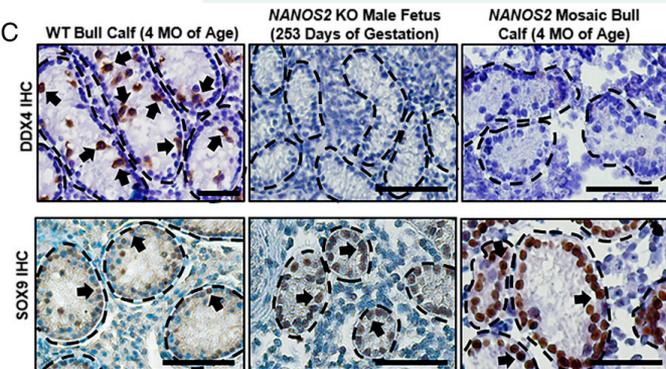


Case studies: cattle

Case 1: surrogate sires – Nanos2 knockout

- Sires with testicles without native spermatogonial stem cells
 - Knockout of *Nanos2* gene by deleting base pairs:
 - To silence the protein required for generation and self renewal of spermatogonial stem cells - no sperm
 - Testicular architecture preserved



Arrows:
 DDX4: germ cells
 SOX9: Sertoli cells

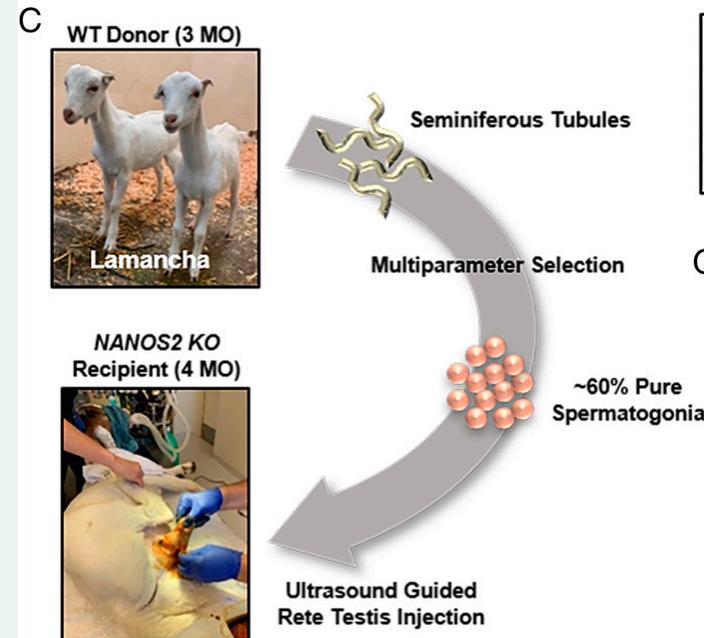
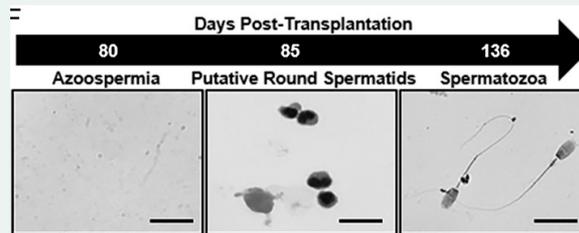
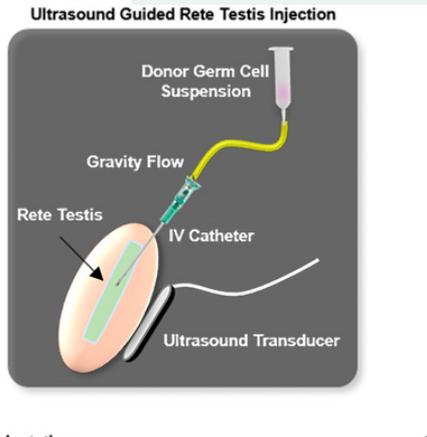


Knockout calf

Michela Ciccarelli^{1,2,3}, Mariana I. Giassetto^{4,5}, Deqiang Miao^{6,7}, Melissa J. Oatley^{8,9}, Colton Robbins^{4,5}, Blanca Lopez-Bladeau^{1,2,3}, Muhammad Salman Waqas¹⁰, Ahmed Tibary^{11,12}, Bruce Whitelaw¹³, Simon Lillo^{14,15}, Chi-Hun Park¹⁶, Ki-Eun Park¹⁷, Bhanu Telugu¹⁸, Zhiqiang Fan¹⁹, Ying Liu²⁰, Misha Regouski²¹, Irina A. Polejeva²², and Jon M. Oatley^{4,5}

Testicles of knockout male as recipients for donor cells

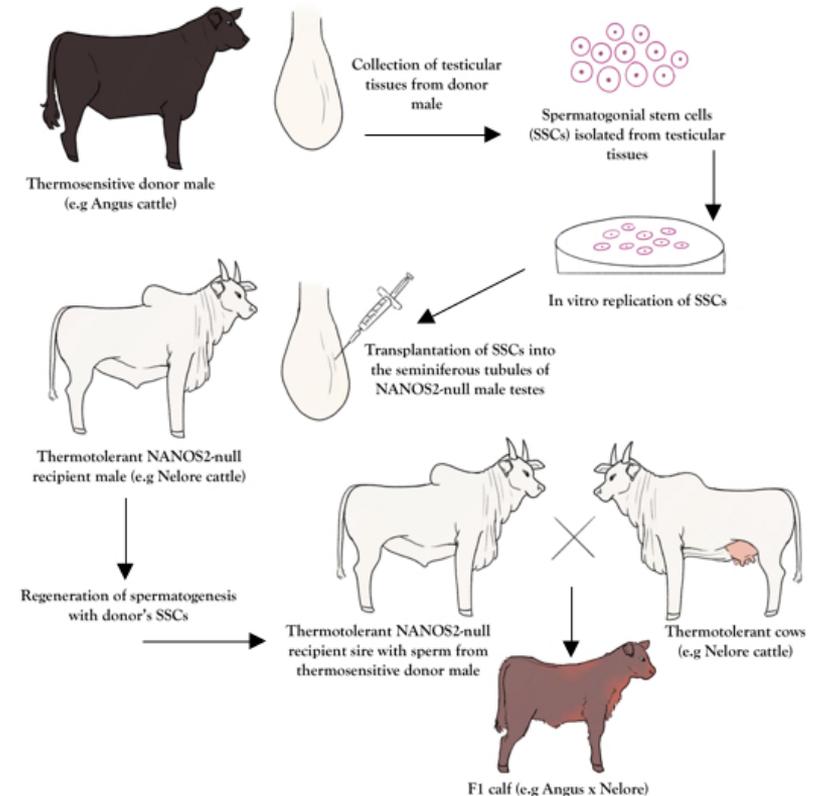
- Spermatogonial stem cells (SSC) collected from young males (donors)
 - Transplanted to seminiferous tubules of recipient testis.
 - Sperm derived from spermatogonial stem cells donors



Knockout males carrying on sperm from another breed

Knockout males from heat-resilient breed with sperm from heat-sensitive breed

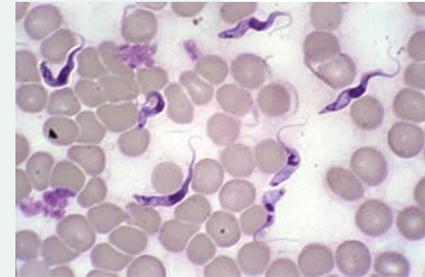
- Surrogate sires could be useful for natural mating in regions where thermo-sensitive breeds that can not stand heat
 - Zebu surrogate sire with Angus sperm



Case 2: trypanosomiasis-resistant knockout cow

African trypanosomiasis caused by extracellular protozoan parasite

- Trypanosoma – transmitted by Tsetse flies
- Chronic debilitating and fatal disease
 - Severe loss of weight



N'Dama – a trypanotolerant breed in Africa

- Animals with reduced parasitemia and anemia when infected



Case 2: trypanosomiasis-resistant knockout cow

Quantitative Trait Loci (QTLs) has identified some genomic regions associated to trypanotolerance in some N'Dama breeds

- With some candidate genes and SNPs

Sequence variants found in those candidate genes could be inserted in trypano-sensitive breeds

Machos receptores para sêmen de animais de interesse

Aplicações potenciais

- Machos nocaute *Nanos2* próximos à puberdade, mas sem mérito genético
 - Receptores de células tronco espermatogoniais de bezerros de alto mérito genético
 - Antecipar produção de sêmen
 - Principalmente em raças com puberdade tardia
 - Uso na monta ou IA
 - Cópia de segurança (back-up)
- Necessário avançar na pesquisa com transplante de células tronco espermatogoniais - até qual idade do doador e do receptor para transplante?



Agradecimentos



Muito obrigado

