

Grupo Miguel Torres
Grupo 9 (Madrid 2)

Reunión TERCEL
Universidad Miguel Hernández, 29 Noviembre 2007

Especificación y autorenovación de los linajes endotelial y hematopoyético

Cati Ana Rosselló

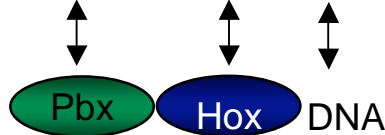
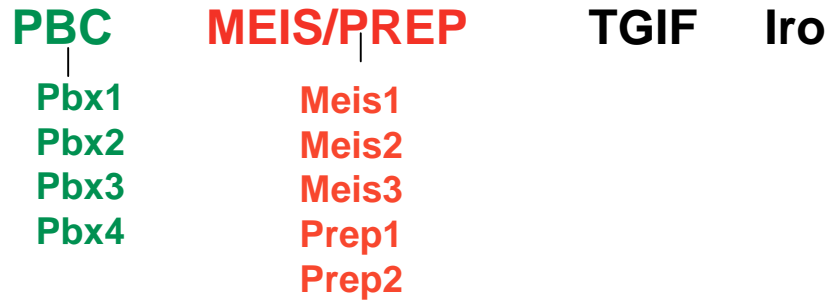
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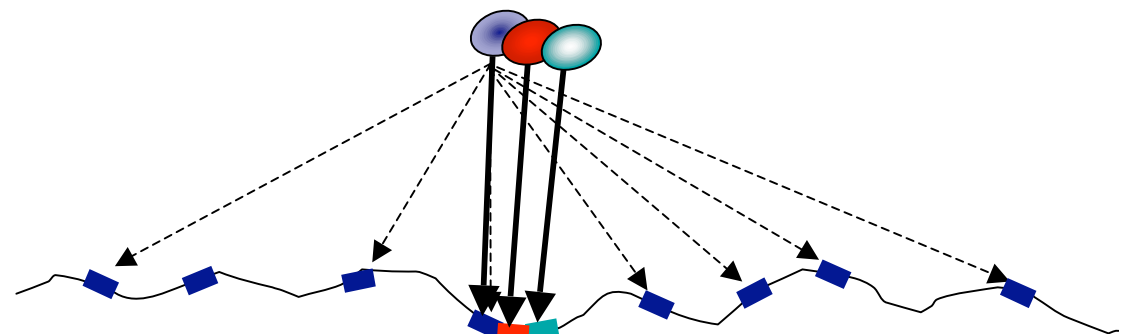
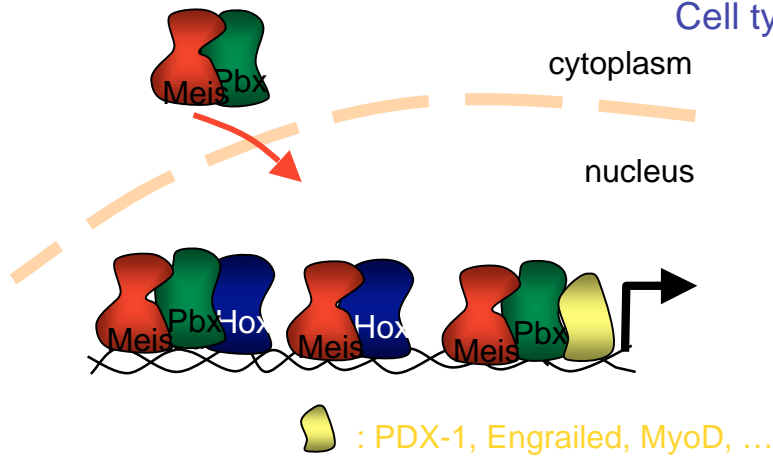


Meis1 gene (Myeloid Ecotropic viral Insertion Site)

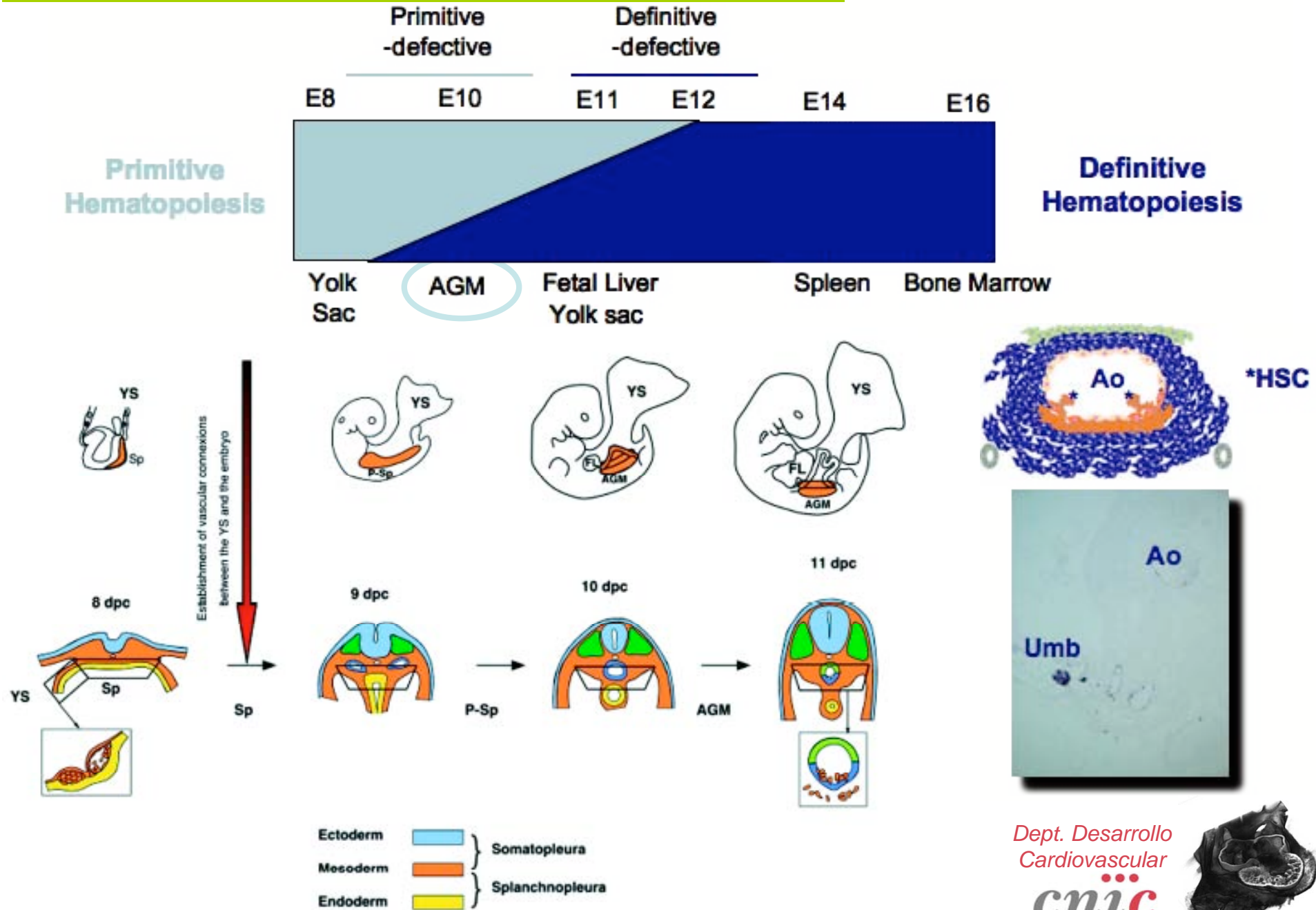
TALE homeobox transcription factors



Regional specification
 Cell type specification
 Differentiation



The origin of definitive HSCs in the amniote embryo

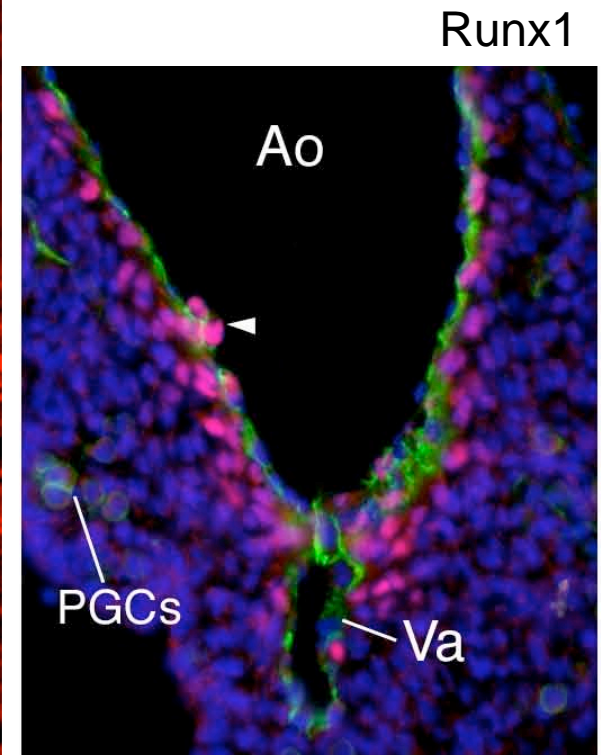
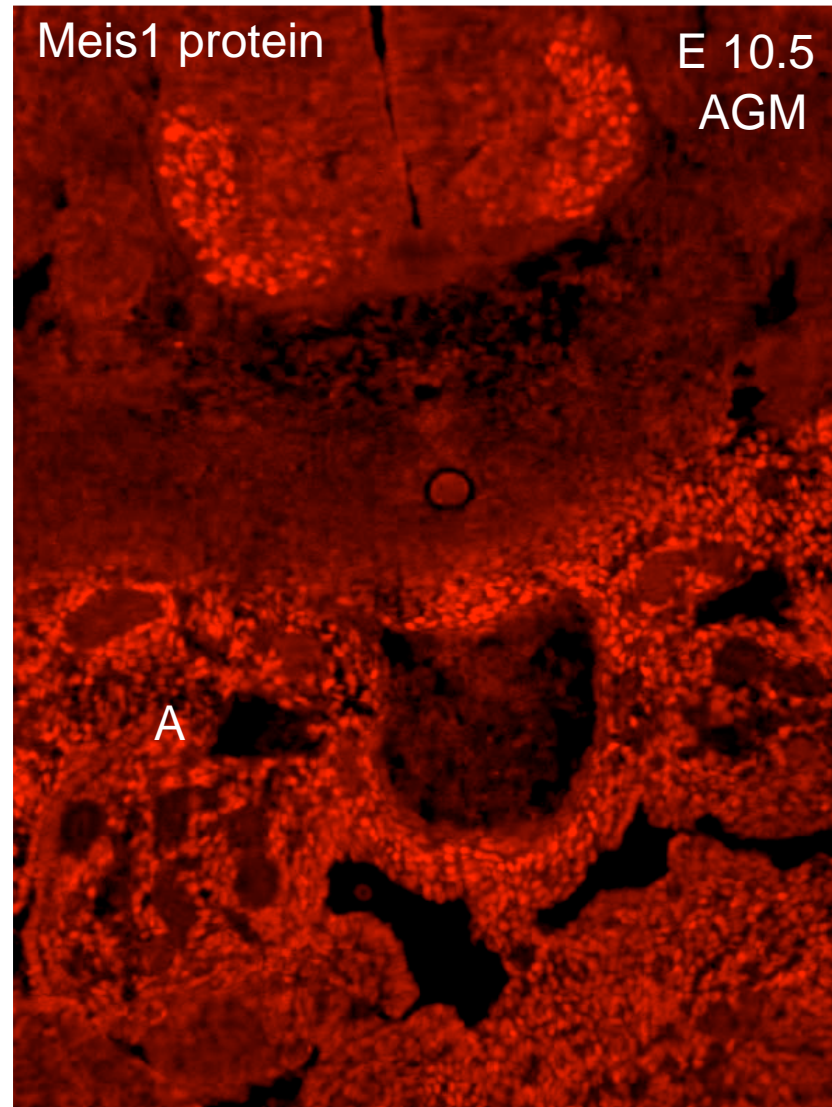
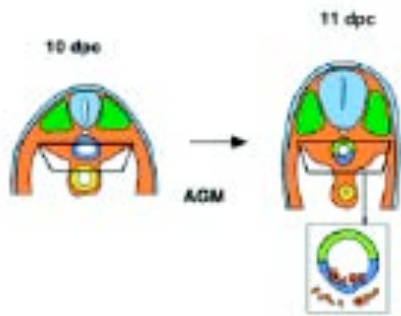


Godin & Cumano *Int J Dev Biol* 2005

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Meis1 is expressed in AGM region

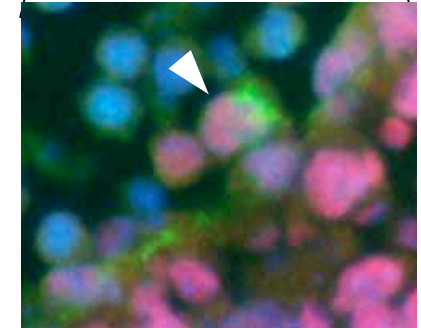
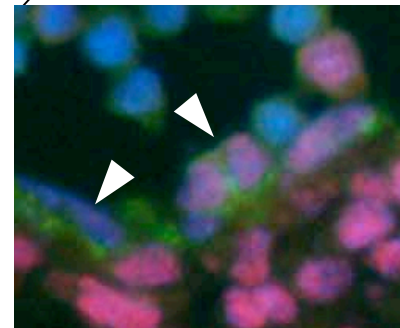
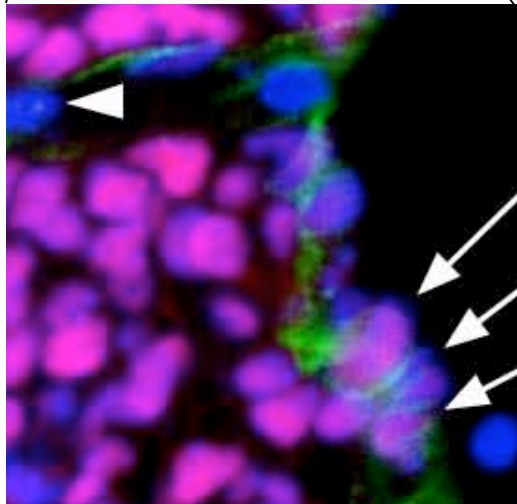
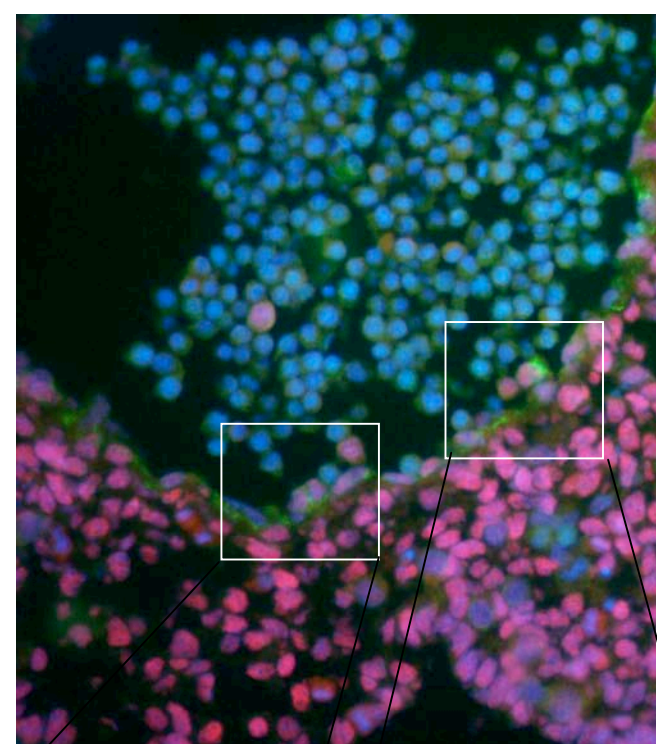
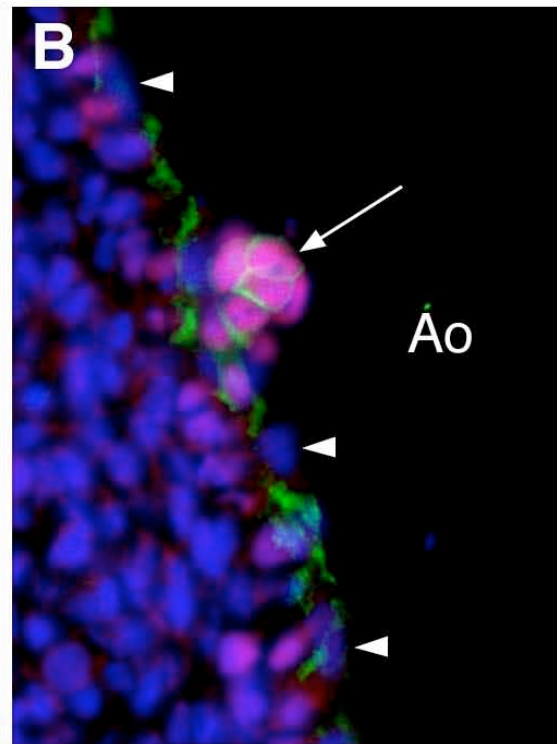
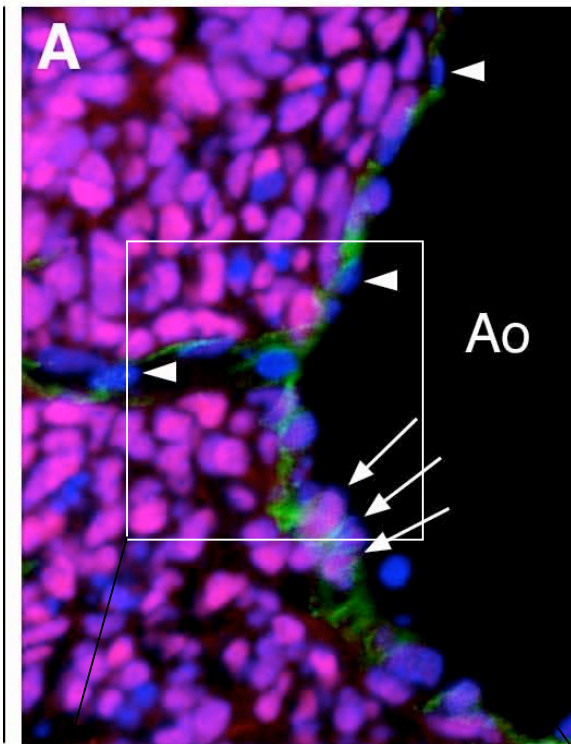


Pbx1 is expressed in AGM region

Meis1

Runx1

Pbx1



Role of Meis1 and its partners Hox and Pbx in HSC specification and self-renewal

Meis1, Pbx and Hox overexpression in mice and humans leads to various types of leukemias.

Hox overexpression immortalizes hematopoietic precursors.

HoxB4 overexpression confers definitive HSC character to differentiating ES cultures.

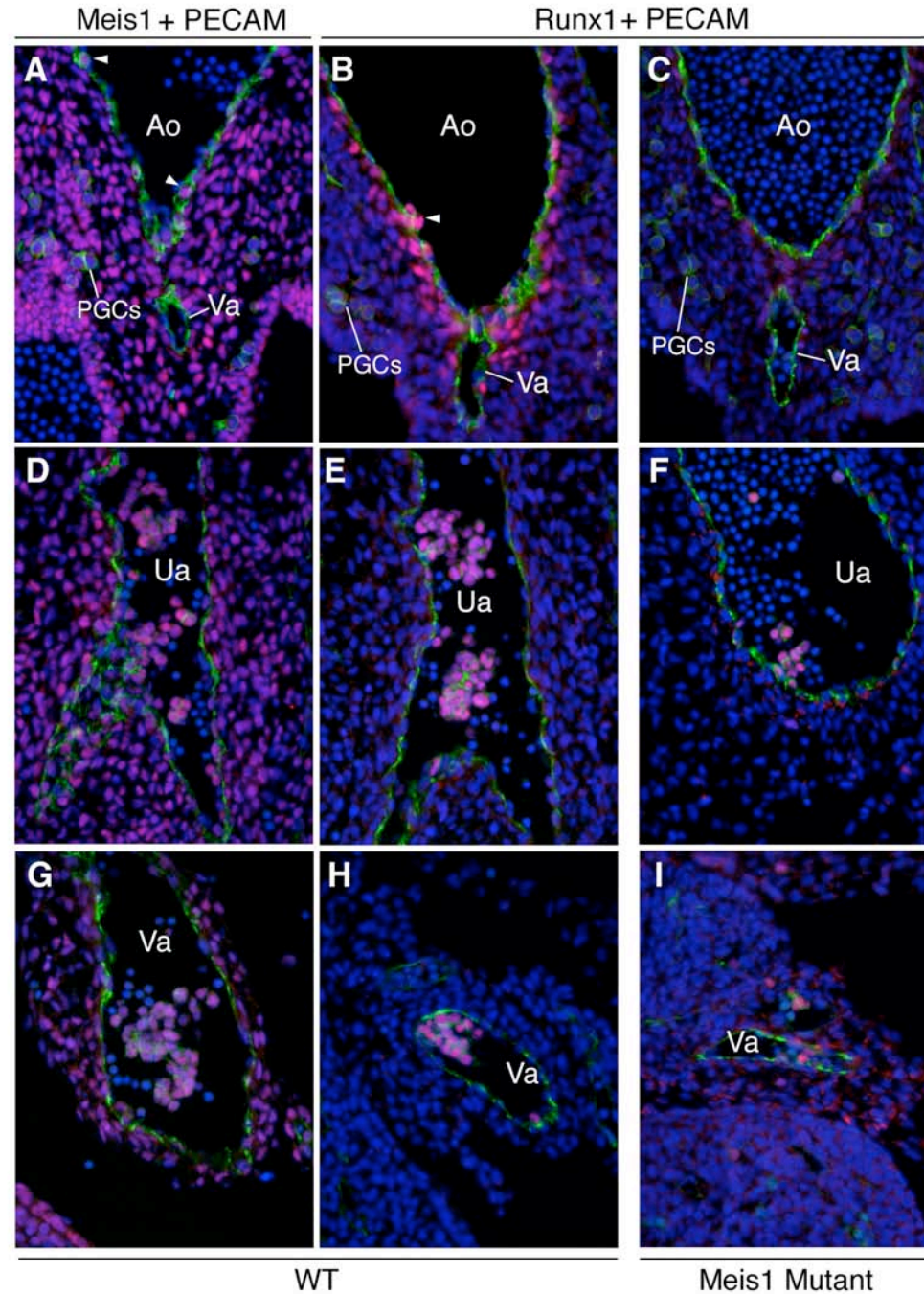
However, no Hox mutant is defective in HSCs.

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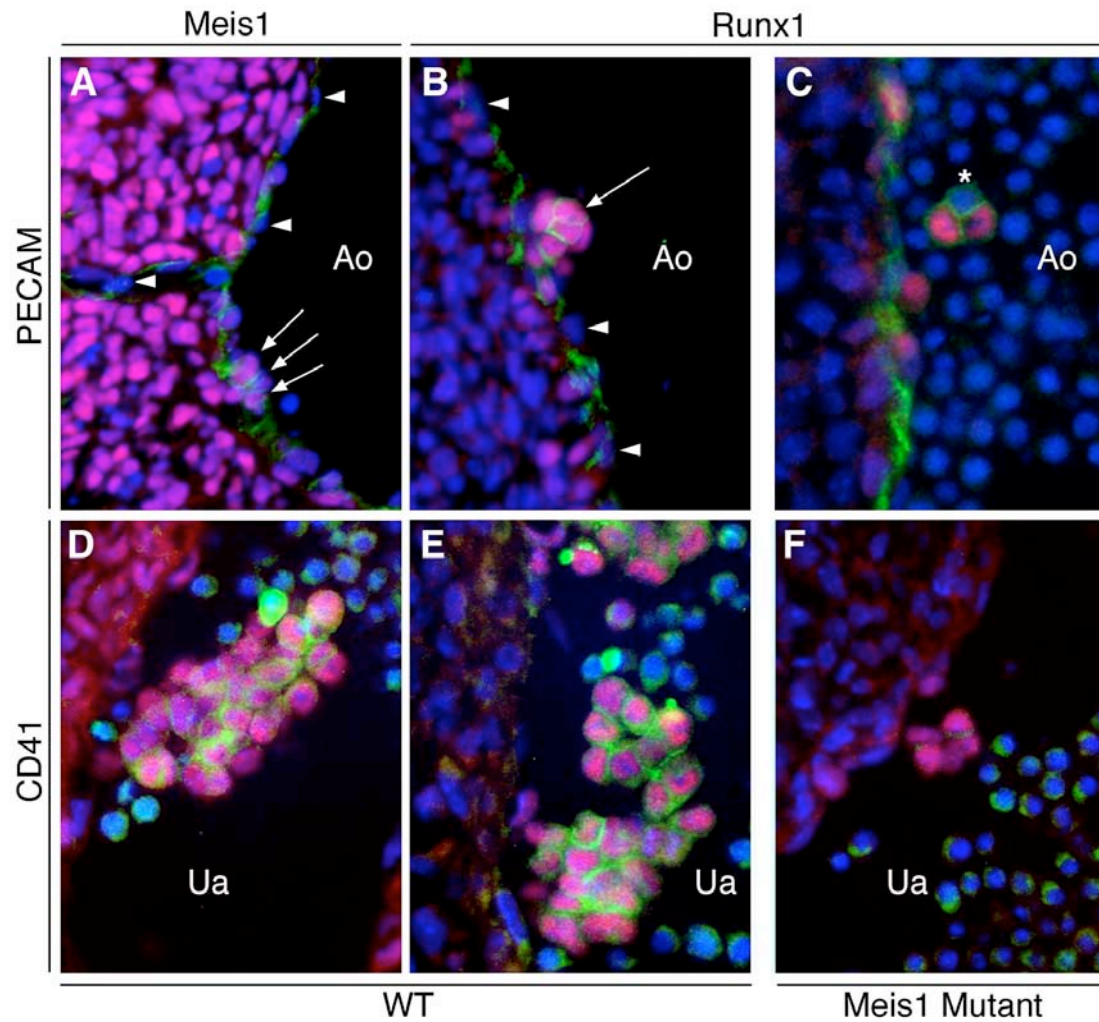
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Alterations in hemogenic activity in *Meis1* mutant mice

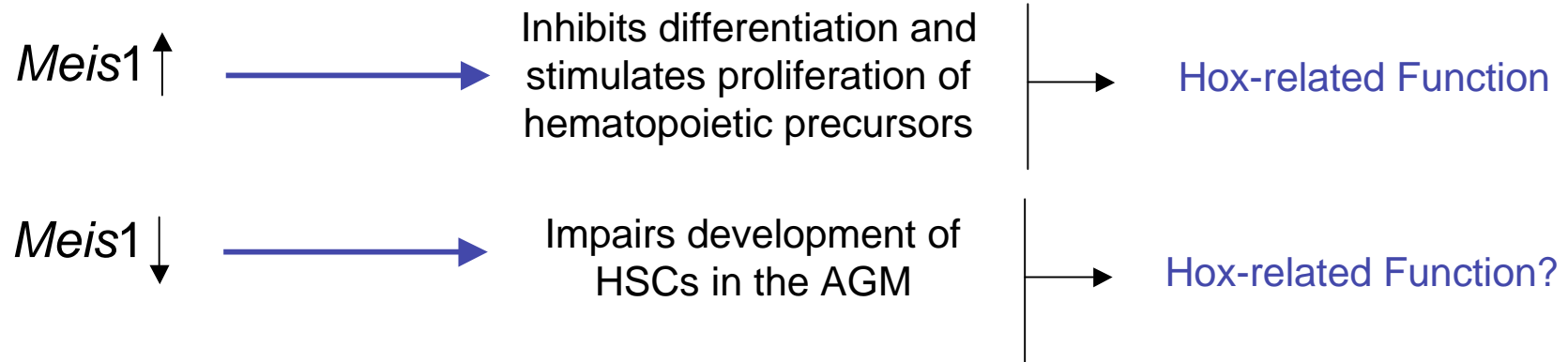


Meis1 is required for HSC clusters development and CD41 expression in HSC

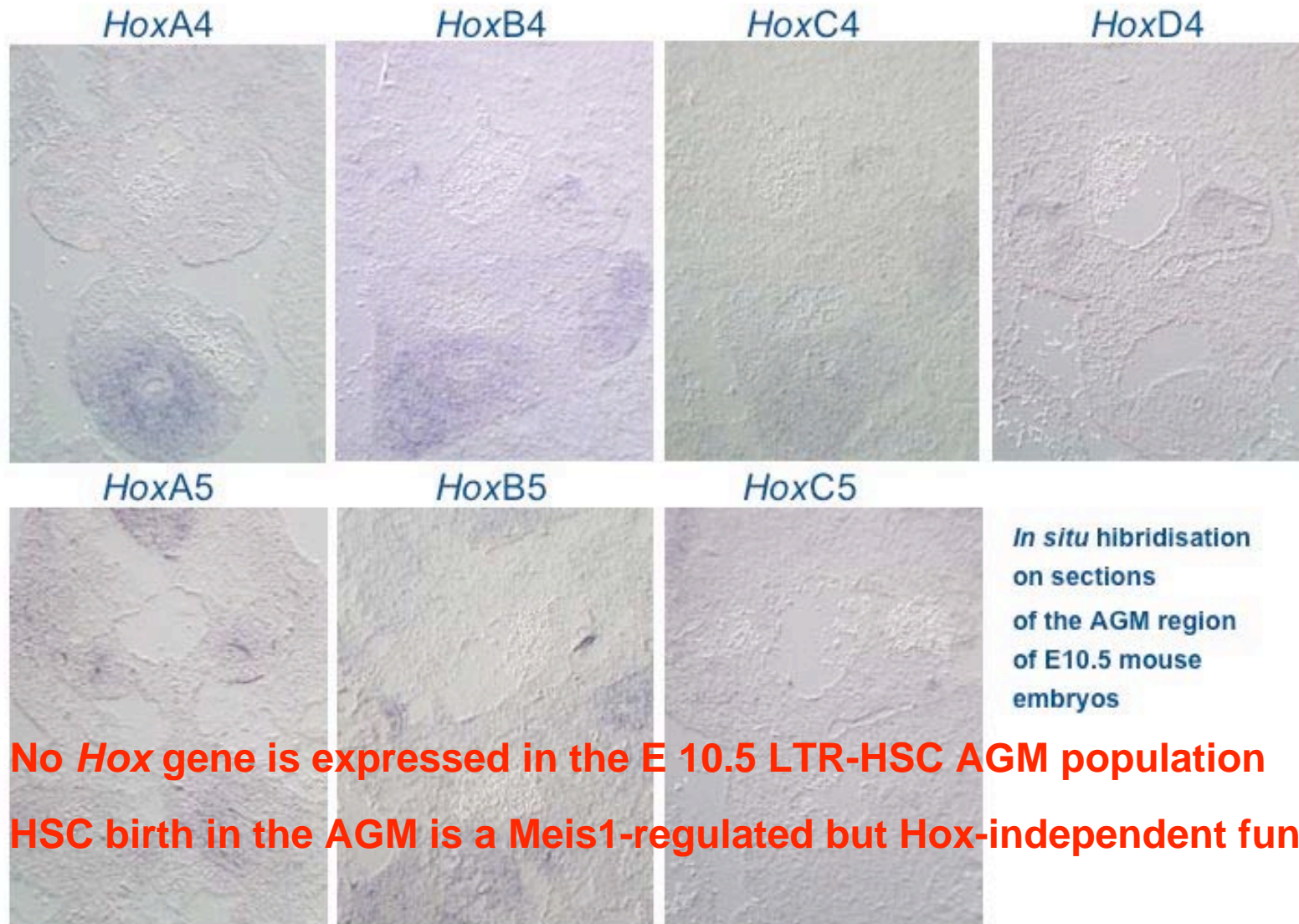


Meis1 is essential to specify definitive HSCs in the AGM

Meis1 might be important to establish the HSC versus the endothelial program



Hox genes expression pattern in AGM



No *Hox* gene is expressed in the E 10.5 LTR-HSC AGM population

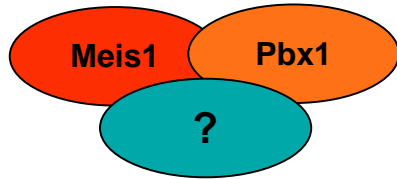
HSC birth in the AGM is a *Meis1*-regulated but *Hox*-independent function

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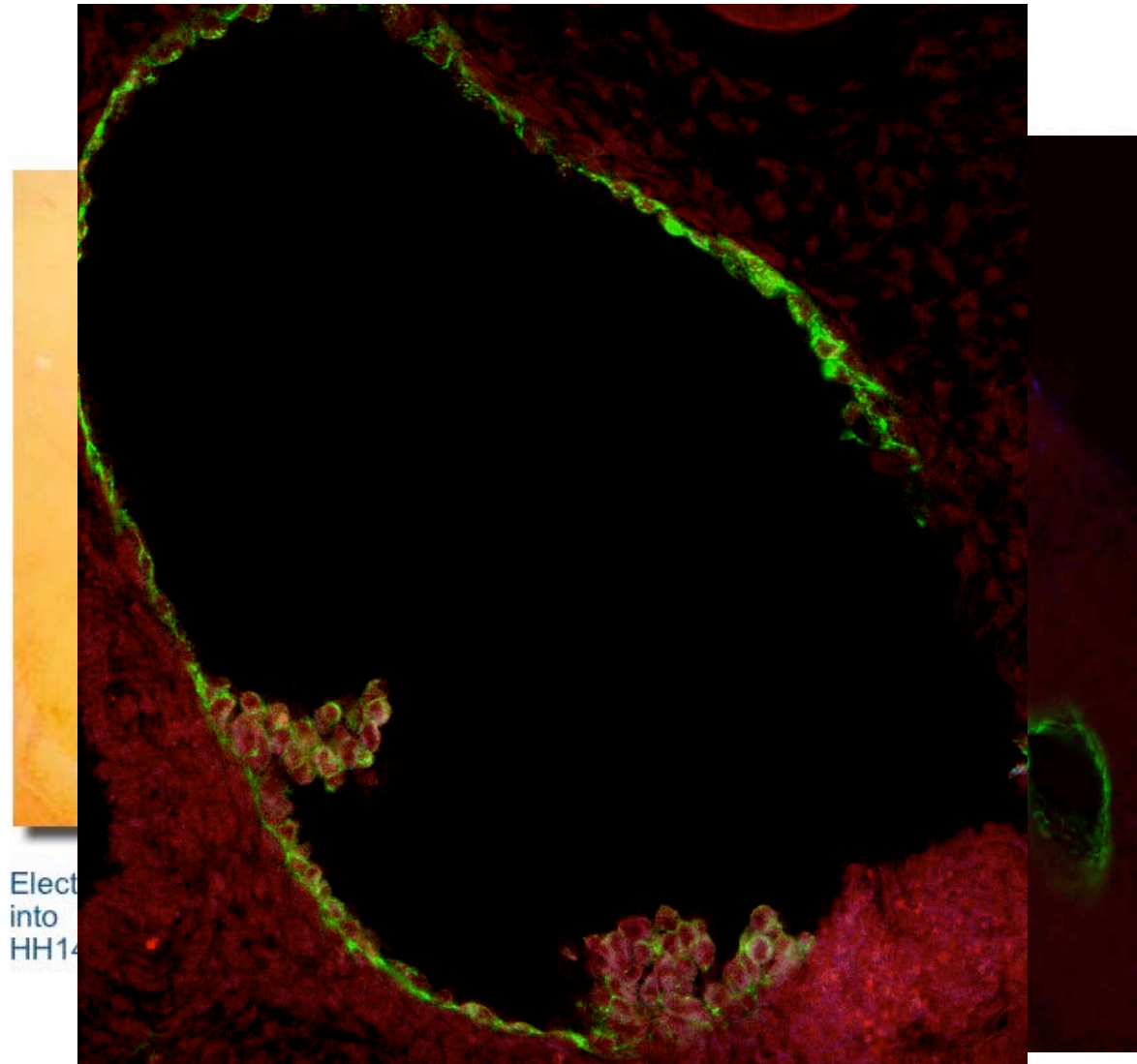
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Identifying functional partner of Meis1 in the aortic hemangioblast



- Lmo2
- Runx1
- SCL/TAL
- GATA-2
- C-myb
- Fli1
- sox17
- .
- .



AGM

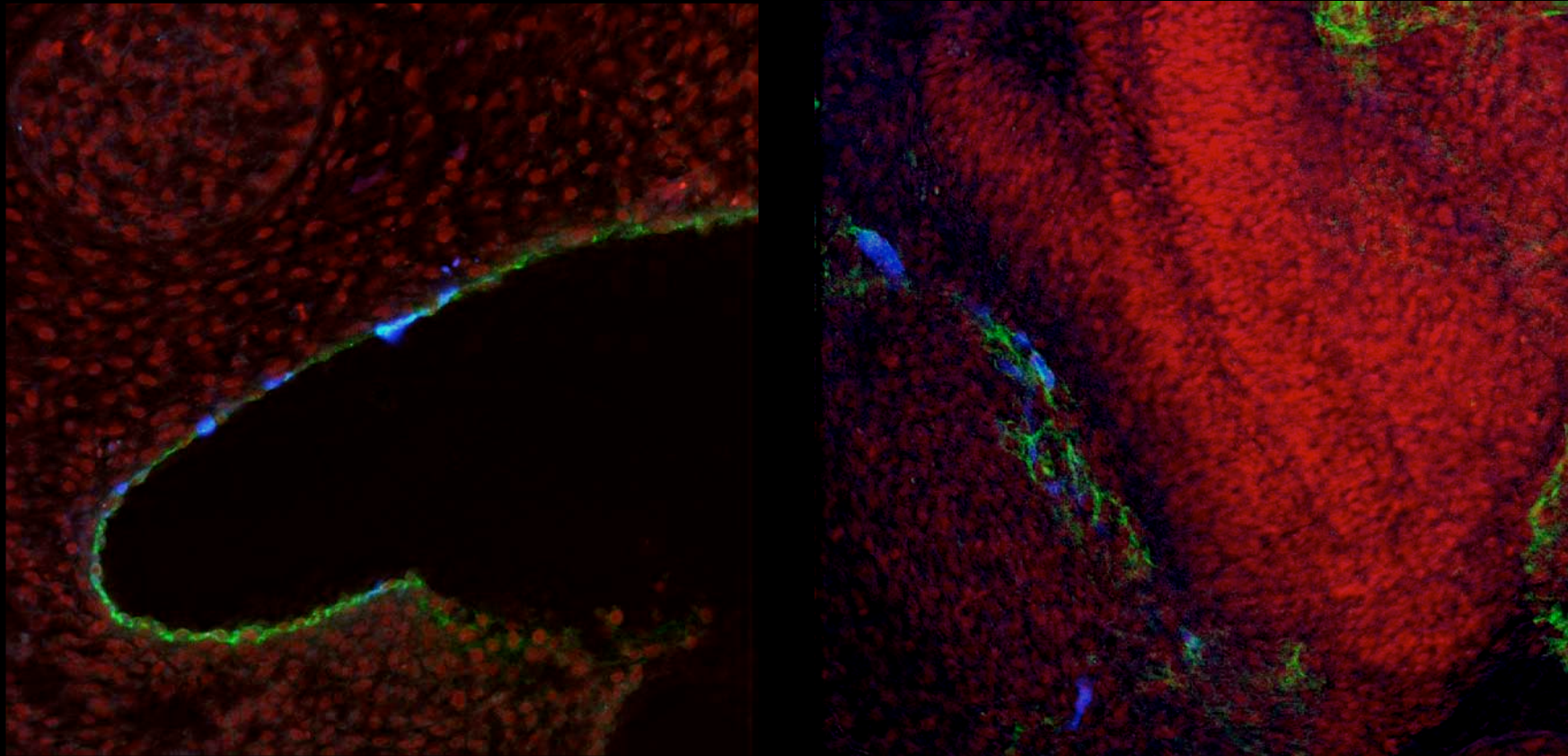
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Meis1+ *Pbx1* overexpression

HH16+24h

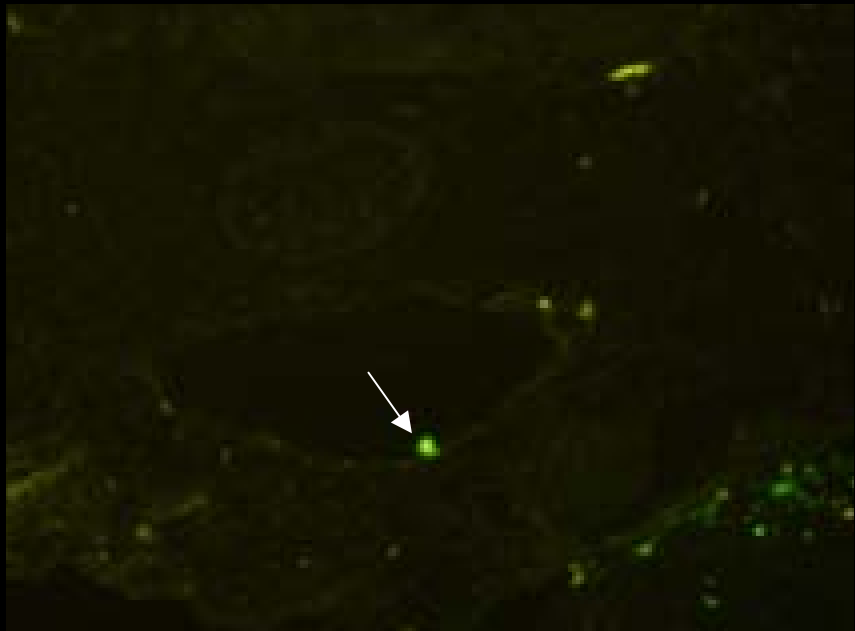
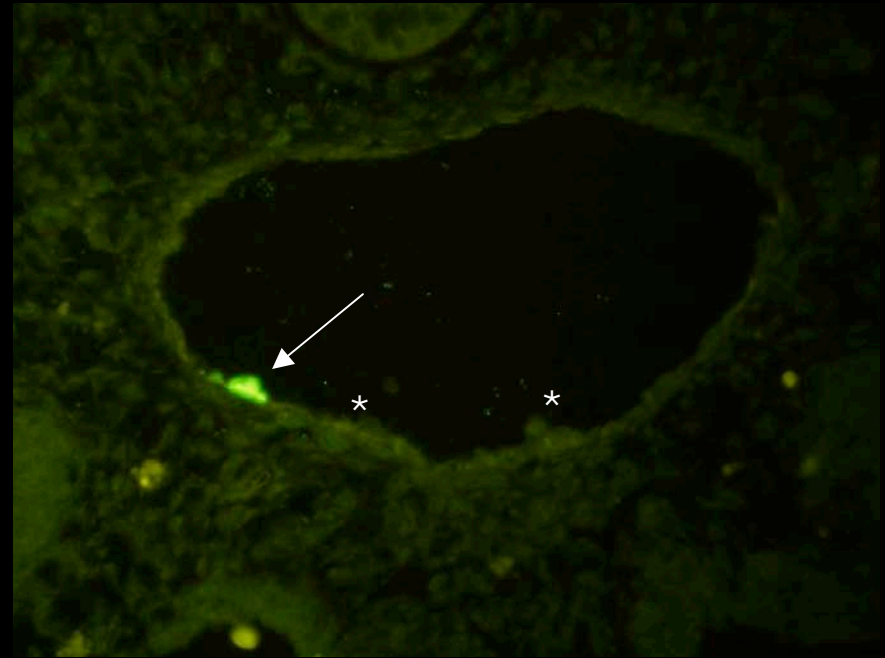


Roof of Dorsal Aorta

Meis1+ Pbx1 overexpression

HH16+24h

Floor of Dorsal Aorta



In summary...

HSC birth in the AGM is a Meis1/Pbx-regulated but Hox-independent Function

Meis1/Pbx activity in dorsal aorta hemogenic endothelium promotes the HSC fate

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Fundación **pro**cnic