

CDH 2024

Congenital Diaphragmatic
Hernia International Symposium
Lille, France

CDH 24 – Lille - La session “Fœtus”



FIMATHO

Filière des maladies rares abdomino-thoraciques



**European
Reference
Network**

for rare or low prevalence
complex diseases

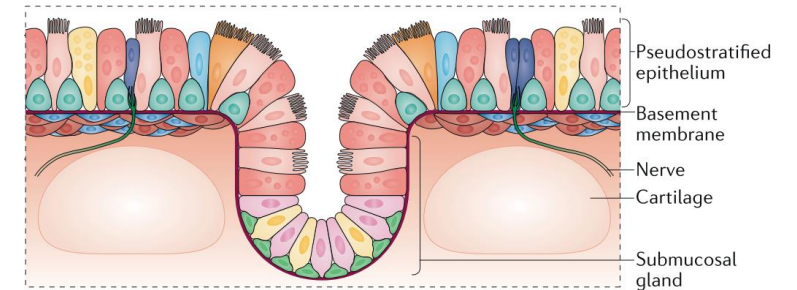
Network
Inherited and Congenital
Anomalies (ERNICA)

Tracheal Aspirate derived basal stem cells as epithelial lung model in CDH- R Wagner

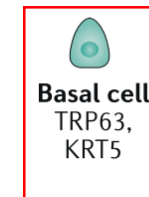


Les cellules souches pulmonaires obtenues par aspiration trachéale sont des substituts pour l'étude du poumon néonatal

- Etat pro-inflammatoire des cellules basales
- Signature pulmonaire protéomique altérée dans le modèle nitrofen et chez l'homme
- Rôle de NF- κ B: facteur de transcription, réponse immune et inflammatoire, contrôle de la prolifération et l'apoptose
- Modification de la différenciation de l'épithélium des voies aériennes normalisée après dexaméthasone ou inhibition spécifique de NF- κ B



Epithelial cell types



Basal cell
TRP63,
KRT5



Secretory (club) cell
SCGB1A1,
SCGB3A2



Multiciliated cell
FOXJ1, TUBB3



Goblet cell
MUC5AC,
MUC5B

Discussion sur corticothérapie systématique, ou pas

Amonkar G, Wagner R, 2022. Cell - STAR Protocols
Wagner R. et al., 2023, AJRCCM
Wagner R. et al., 2023, Annals of Surgery

Fetal heart and CDH: what to expect? D Laux



- La dysfonction cardiaque augmente la mortalité
- Est-ce que l'hypoplasie du VG foetal impacte le pronostic post natal ? Non évalué dans les études existantes
- “The search for a (new) prenatal cardiac prognostic marker is going on
.....It might not exist in the very end”

Lung organoid isolation from amniotic and tracheal fluids

P de Coppi

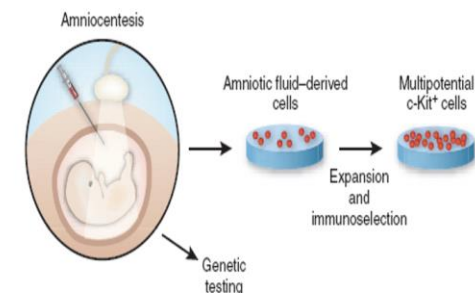
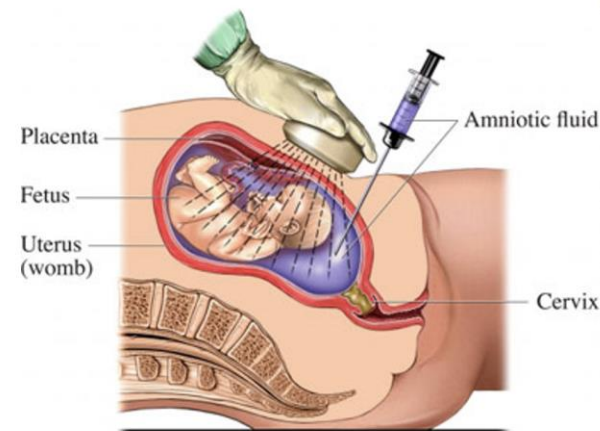


- Est-ce qu'il est possible de générer des organoïdes foetaux humains sans biopsie ?
- Est-ce que cela est faisable dans un temps et avec une technique compatible avec une intervention en prénatale?

Isolation of amniotic stem cell lines with potential for therapy

Paolo De Coppi^{1,3}, Georg Bartsch, Jr^{1,3}, M Minhaj Siddiqui¹, Tao Xu¹, Cesar C Santos¹, Laura Perin¹, Gustavo Mostoslavsky², Angéline C Serre², Evan Y Snyder², James J Yoo¹, Mark E Furth¹, Shay Soker¹ & Anthony Atala¹

2007



Lung organoid isolation from amniotic and tracheal fluids

P de Coppi



nature medicine



Article

<https://doi.org/10.1038/s41591-024-02807-z>

Single-cell guided prenatal derivation of primary fetal epithelial organoids from human amniotic and tracheal fluids

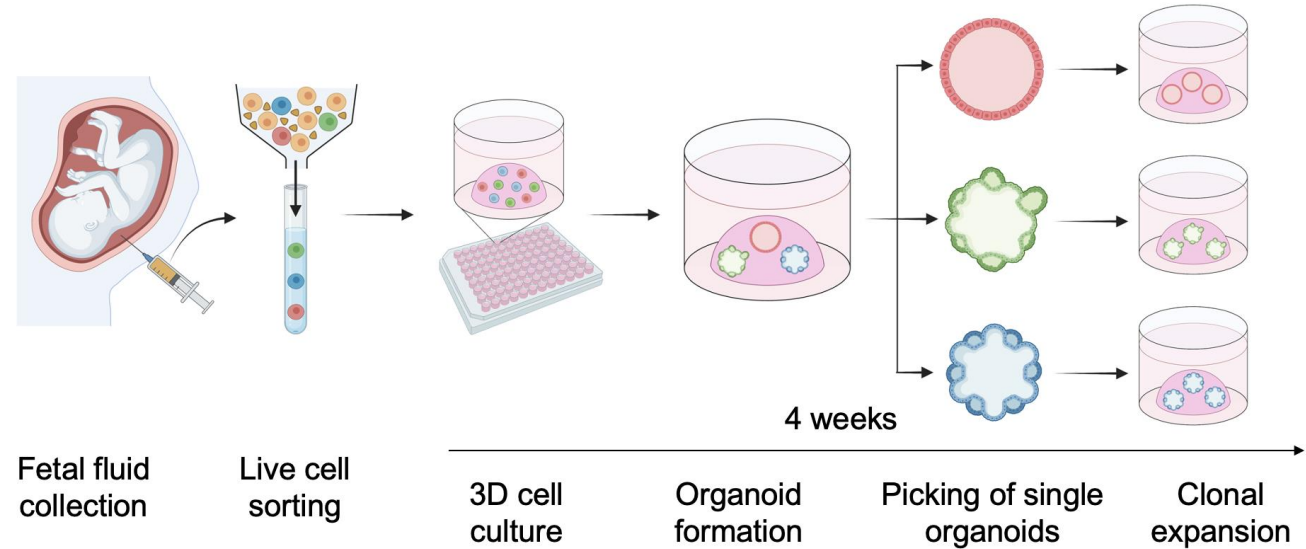
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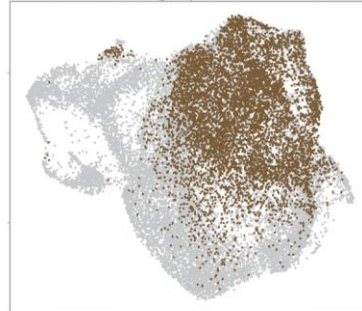
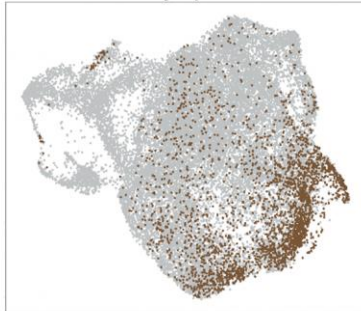
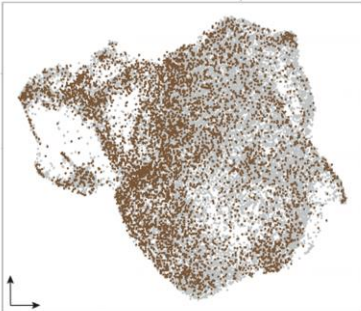
Mattia Francesco Maria Gerli^{1,2,16}, Giuseppe Calà^{1,2,16}, Max Arran Beesley², Beatrice Sina^{2,3}, Lucinda Tullie^{2,4}, Kylin Yunyan Sun^{1,2}, Francesco Panariello⁵, Federica Michielin², Joseph R. Davidson^{2,6}, Francesca Maria Russo⁷, Brendan C. Jones², Dani Do Hyang Lee², Savvas Savvidis⁸, Theodoros Xenakis², Ian C. Simcock^{2,9}, Anna A. Straatman-Iwanowska¹⁰, Robert A. Hirst¹⁰, Anna L. David^{6,7}, Christopher O'Callaghan², Alessandro Olivo⁴, Simon Eaton², Stavros P. Loukogeorgakis^{2,11}, Davide Cacchiarelli^{5,12,13}, Jan Deprest^{6,7}, Vivian S. W. Li⁴, Giovanni Giuseppe Giobbe² & Paolo De Coppi^{2,7,11,14,15}



Gastrointestinal epithelia

Kidney epithelia

Lung epithelia



This work demonstrates that the AF contains tissue-specific fetal epithelial progenitor cells originating from various developing organs. We show that, under defined culture conditions, these cells form epithelial organoids resembling their tissues of origin (small intestine, kidney and lung). Finally, we provide evidence that lung organoids derived from AF and TF of fetuses affected by CDH exhibit features of the disease.

The fetal brain in CDH – F Russo



Prenatal Imaging studies

Delayed maturation

Parenchymal damage

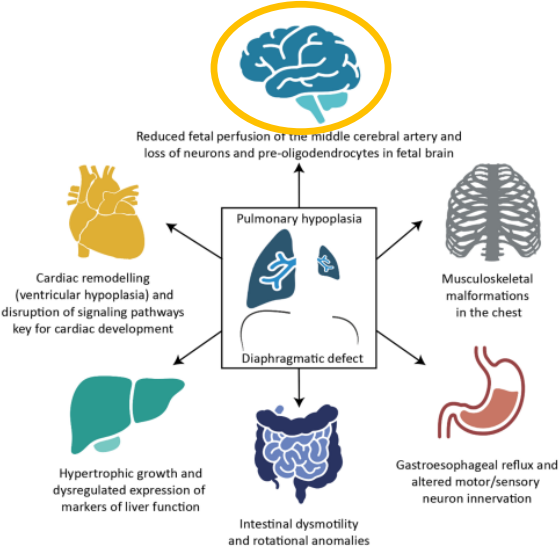


Abnormal vascularization

Modèles animaux

Increased extra-axial fluid space

Increased extra-axial fluid space

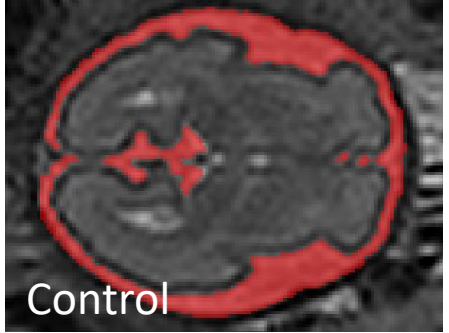
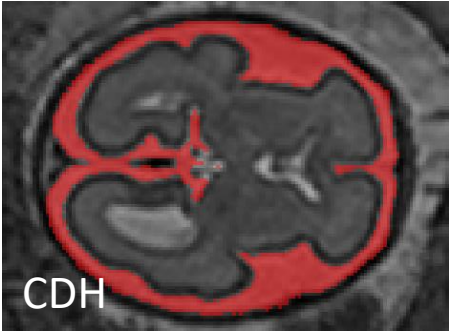


Isolated CDH

Motor function (13%, 2-30%)

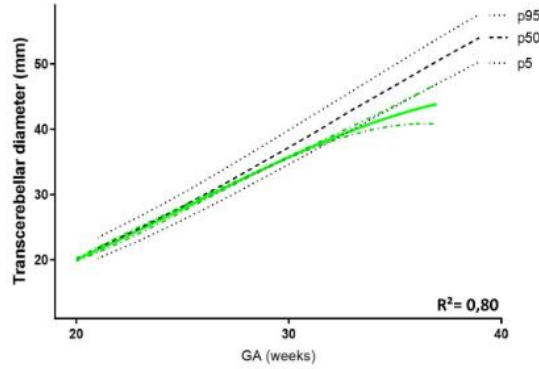
Cognition 5% (13%, 0-20%)

Hearing (3%, 1-7%)



➔ Increased risk of permanent psychomotor delays

Cervelet



The fetal brain in CDH – F Russo



- Cause placentaire ?
- Inflammation ?
- Origine embryologique?

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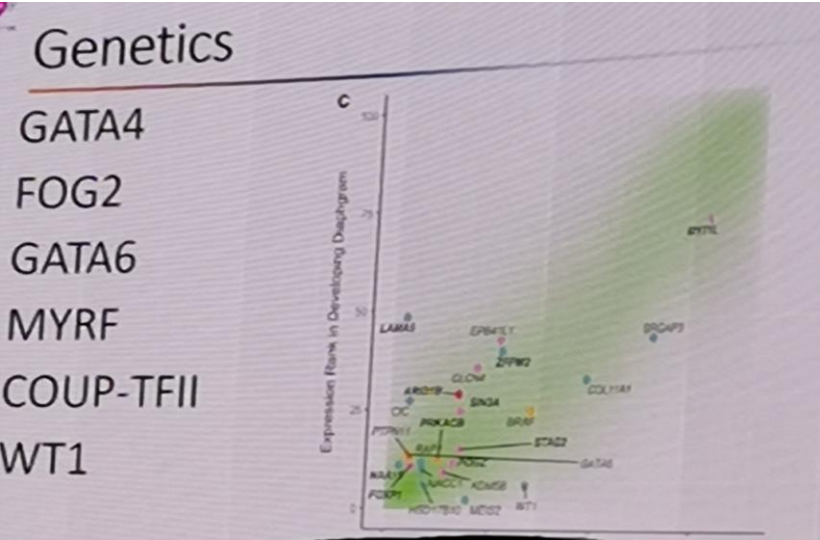
ORIGINAL
ARTICLES



Prenatal Brain Maturation is Delayed in Neonates with Congenital Diaphragmatic Hernia

Sandy Johng, MD¹, Daniel J. Licht, MD², Holly L. Hedrick, MD, FACS³, Natalie Rintoul, MD¹, Rebecca L. Linn, MD⁴, Juliana S. Gebb, MD⁵, Rui Xiao, PhD⁶, and Shavonne L. Massey, MD, MSCE²

Conclusions Prenatal brain maturation in neonates with CDH is delayed. Placental pathology may influence fetal brain development. The etiology and clinical impact of prenatal brain immaturity in neonates with CDH warrant further investigation. (*J Pediatr* 2024;264:113738).



Harting, CDH 2024

GATA4 is a regulator of astrocyte cell proliferation and apoptosis in the human and murine central nervous system

S Agnibotti, A Wolf, D Picard, C Hawkins & A Guha
Oncogene 28, 3033–3046 (2009) | Cite this article

Corticothalamic projection neuron development beyond subtype specification: Fog2 and intersectional controls regulate intraclass neuronal diversity

Maria J. Galazo¹, Jason G. Emsley¹, and Jeffrey D. Macklis^{1,*}
¹Department of Stem Cell and Regenerative Biology, Center for Brain Science, and Harvard Stem Cell Institute, Harvard University, Cambridge, MA, USA

MYRF: A Mysterious Membrane-Bound Transcription Factor Involved in Myelin Development and Human Diseases

Hao Huang¹, Fang Zhou¹, Shiyu Zhou¹, Mengheng Qiu¹

ORIGINAL ARTICLE
The Transcription Factors COUP-TFI and COUP-TFII have Distinct Roles in Arealisation and GABAergic Interneuron Specification in the Early Human Fetal Telencephalon

Ayman Alzu'bi^{1,2}, Susan J. Lindsay², Lauren F. Harkin^{1,2,3}, Jack McIntyre^{1,2}, Steven N. Ligo² and Gavin J. Clowry¹

The fetal brain in CDH – F Russo

