Imaging Genomics
David Edwards,
Evelina London Children’s Hospital.
The Fetal Context

18 GW

25 GW

36 GW

Twins

(Hayat et al AJN, 2011)
Magnetic Resonance Imaging of the Preterm Brain

24 weeks gestation

Term

(Battin et al Lancet 1997;349:1741)
Brain growth during neonatal intensive care

Structural connections: the wiring diagram of the brain

- White matter tracts carry information

- Visualised in live humans using diffusion Magnetic Resonance Imaging (dMRI)
Constrained spherical deconvolution tractography

Images Donald Tournier, Max Pietsch
Neonatal arcuate fasciculus related to language skills at 20 months.

Salvan et al, Human Brain Mapping 2017
Imaging genetics

- Extracting information from data:
- Moving from physics to biology using genetics
Candidate genes associated with white matter abnormality in preterm infants (n=72)

Boardman et al, Pediatrics 2014
Genetic Imaging: gene pathways with significant linkage to reduced white matter development in preterm infants

<table>
<thead>
<tr>
<th>Pathway name</th>
<th>Adjusted for PMA</th>
<th>Adjusted for GA PMA</th>
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<td>Ppar Signaling Pathway</td>
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<td>Glycerolipid Metabolism</td>
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<td>Alpha Linolenic Acid Metabolism</td>
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<td>Glycosylphosphatidylinositol Gpi Anchor Biosynthesis</td>
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<td>Phosphatidylinositol Signaling System</td>
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Krishnan et al, Brain Behav 2016
Replication study n=272
ePrime cohort
Whole brain connectivity matrix
Top 100 SNP associated with imaging phenotype: 47 genes
PPARG expression in human brain

Source: Allen Brain Atlas

Krishnan et al. Proc Nat Acad Sci USA 2017
Frequency of participation of cortical regions among the top 100 ranked tracts

Significant over-representation of Insular Cortex

Krishnan et al. Proc Nat Acad Sci USA 2017;114:13744-9
PPARγ pathway

- Growth Factor
- Growth Factor Receptor
- Intracellular fatty acids and metabolites (Prostaglandins, PGJ₂)

Modifiers:
- JNK
- ERK
- MKP

Co-Activators:
- RXR
- CBP
- SRC-1

PPARγ

PPRE

Target Genes
- COX2
- IL1
- TNF
- aP2
- ADRP
- LPL
- Adipo
- C/EBP

Decreased inflammation

Adipocyte differentiation
Increased lipid storage
Antidiabetic effects

Biological Response
Recognition and thanks

- Daniel Rueckert
- Jo Hajnal
- Steve Smith
- Serena Counsell
- Paul Aljabar
- Gareth Ball
- Maria Murgusova
- Emma Robinson
- Kanwal Bhatia
- Mary Rutherford
- Tom Arichi
- Jelena Bozek
- Dafnis Batalle Bolero
- Ahmed Serag
- Sui Jiang
- Shona Falconer
- Andrew Chew
- Antonis Makropoulos
- Nora Tusor
- David Cox
- Giovanni Montana
- Julio Ferrazzi
- Max Pietsch
- Emer Hughes
- Fran Padormo
- Donald Tournier
- Valentina Doria
- Hilary Toulmin
- Jeff Hand
- Ioannis Gousias
- Anand Pandit
- Fran Padormo
- Anthony Price
- Lorenzo Fabrizi
dHCP research nurses, radiographers, midwives and research assistants

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