step consists on testing the effects of drugs in vitro in cell lines and in vivo in mouse xenografts.

To translate the results of this research into the clinical scenario the program includes the development of phase I-II trials. Considering that cancers in children are different from tumours of adults we need to test new drugs in early phase clinical trials specifically designed for children.

In summary, the promotion of early clinical research in children with cancer combined with a better knowledge of the tumour biology will allow a more effective introduction of new targeted therapies into the clinical practice.

Pulmonology

15-018 NEW THERAPIES FOR PULMONARY HYPERTENSION AND BPD – FROM BENCH TO BEDSIDE
S Kourembanas, K Sdrimas, Cj Lee, G Hansmann, A Fernandez-Gonzalez, SA Mitsialis. Division of Newborn Medicine, Boston Children’s Hospital, Boston, USA
10.1136/archdischild-2014-307384.18

We have used mesenchymal stem cells in preclinical models of pulmonary hypertension (PH) and in the hyperoxia-induced neonatal murine model of bronchopulmonary dysplasia (BPD) to suppress inflammation and improve survival while attenuating alveolar injury and PH. The protective effect was predominantly mediated by paracrine mechanisms, since, cell-free MSC-conditioned media were even more efficacious than MSCs in preventing or reversing established disease. The active moieties that confer the therapeutic efficacy of MSCs remain elusive but likely include secreted proteins, nucleic acids, and membrane components, all potentially packaged in MSC-released microvesicles. We have shown that such particles, a class of which is represented by exosomes, convey the therapeutic efficacy of MSCs in the murine hypoxic model of PH. Exosome treatment was also able to abrogate early hypoxic macrophage influx and downregulate hypoxia-activated inflammatory pathways, thus recapitulating the well-characterised, anti-inflammatory properties of MSCs. The clinical use of MSCs in several on-going trials or the MSC secretome (e.g. exosomes) is a budding new field that represents an exciting and promising approach to therapeutic interventions for diseases of the lung.

Pulmonology Symposium (Supported By and Unrestricted Educational Grant from Chiesi).

15-019 THE EMERGENCE OF CONSCIOUSNESS
H Lagercrantz. Astrid Lindgren Children’s Hospital, Karolinska Institute, Stockholm, Sweden
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The first breaths of air have since antique time been regarded as the ignition of life as indicated by the word spirits. The newborn becomes animated in this way – i.e. the emergence of consciousness. In modern time a bioethics committee1 has stated that when the newborn encompasses the capacity to breathe either independently, or with the support of a ventilator is the moral and legal point when human life must be preserved independent of gestational age. Awakening at birth is crucial for being conscious. This is triggered by the stress of being born i.e. mobilisation of catecholamines, cooling due to evaporation of the amniotic fluid...
and removal of placental suppressors when clamping the cord. The locus coeruleus is activated causing the arousal.

A spontaneous resting state activity has been found in newborn infants with fMRI. This activity may correspond to the idea of William James that there is a "stream of consciousness". It involves five hubs including the somatosensory system and the auditory and visual cortex in the infants. This is in contrast to adults where ten hubs were defined including the insula, prefrontal cortex and ventromedial prefrontal cortex. Thus the infant is probably only aware of what it feels, sees and hears in present time, while the adult relates the sensory input to memories, itself and also plans for the future.

**REFERENCES**


**IS-020 FUNCTIONAL CONNECTIVITY IN THE INFANT BRAIN**

CD Smyser, Neurology and Pediatrics, Washington University, St. Louis, USA

Advanced MRI techniques have been increasingly applied in infants to explore the structural and functional architecture of the developing brain. Functional connectivity magnetic resonance imaging (fcMRI) utilises spontaneous, low-frequency, coherent fluctuations in blood oxygen level dependent signal to identify networks of functional cerebral connections. Application of fcMRI in infants provides unique technical challenges. To obtain high-quality fcMRI data, investigators have applied new technology and modified acquisition practices. Advanced analysis techniques have also been developed to improve anatomic registration, eliminate artifactual variance and improve signal-to-noise ratios. These measures have enabled successful, robust fcMRI investigations in neonates. Importantly, these methods are transferable across institutions and clinical populations of interest.

Neonatal fcMRI investigations have included healthy, term-born infants and prematurely-born infants with and without cerebral injury. In these populations, fcMRI data has been used to identify immature networks as early as 26 weeks postmenstrual age. These networks gradually mature. Prematurity (Figure 1) and white matter injury (Figure 2) significantly affect connectivity, altering network configuration and strength. These results demonstrate the promise of fcMRI as an investigational tool of neurodevelopment, providing insight into the earliest forms of functional cerebral development. While key groundwork has been laid, additional efforts are necessary to apply continued advances in technology and methodology. Expanded investigations will provide greater understanding of the processes underlying typical and atypical cerebral development and the role of these networks in neurodevelopmental outcomes.

**IS-021 FUNCTIONAL MRI AND LANGUAGE DEVELOPMENT IN INFANTS AND CHILDREN**

I Krägeloh-Mann, K Lidzba. Pediatric Neurology, University Children’s Hospital, Tübingen, Germany

Language is specific to the human and can, thus, not be studied in the animal. In the adult, there is a strong dominance of the left hemisphere for most aspects of language and stroke in language regions often leads to permanent aphasia. In contrast, lesions in similar locations acquired very early do not lead to an impaired language function in the affected child.

With the advent of fMRI, the cerebral representation of language organisation can now be studied non-invasively even in smaller children.

**Questions**

1. Language representation during development?
2. Early left hemispheric lesions and language representation?
3. If there is language reorganisation, does it affect right hemispheric functions?
4. How good is right hemispheric language?
5. What is the time frame for reorganisation?

**Answers**

1. Language representation is initially bilateral and increasingly left dominated during development.