University of Birmingham

Cerebrospinal Fluid Disorders Research Group

Group leader: **Dr Alexandra Sinclair (/staff/profiles/cem/NN/sinclair-alexandra.aspx)**

Overview

Cerebrospinal fluid (CSF) bathes the brain and spinal cord and is vital for the maintenance of fluid homeostasis within the central nervous system. Understanding the pathophysiology of CSF disorders is key to improve its diagnosis and management as well as to develop novel therapy approaches.

Our research group

Cerebrospinal fluid is continuously produced by the choroid plexus in the lateral, third and fourth ventricles. It flows through the ventricular system, draining through basal cisterns of the brain, bathing the spinal cord and then reabsorbed into the blood circulation.

The production of CSF by the choroid plexus is tightly regulated providing the necessary nutrients and removing any waste which may compromise the normal homeostasis of the central nervous system. Because the CSF bathes the brain and spinal cord, it provides buoyancy protecting them from trauma. The CSF is vital for the maintenance of a stable intracranial pressure by compensating for changes of increased intracranial blood pressure.

Our research group is thus interested in understanding the molecular, cellular and physiological mechanisms underlying CSF disorders. The ultimate aim is to develop strategies to improve diagnosis, management and development of novel therapeutic approaches.

Our research group has a diverse range of interests which include evaluation of intracranial pressure dynamics, particularly focusing on idiopathic intracranial hypertension; development of chronic communicating hydrocephalus after subarachnoid haemorrhage; Growth factors and novel peptide hormones in fluid homeostasis; management and outcome of post-traumatic syringomyelia.

Open all sections

Current Projects

- Sustained treatment of Idiopathic Intracranial Hypertension (IIH) through weight loss induced by bariatric surgery.
- Assessing the therapeutic efficacy of an 11beta-hydroxysteroid dehydrogenase type 1 inhibitor (AZD4017) in idiopathic intracranial hypertension (IIH).
- The role of steroid hormones and 11beta hydroxysteroid dehydrogenase type 1 in intracranial pressure regulation in collaboration with Professor Paul Stewart (CEDAM, School of Clinical and Experimental Medicine).
- Creation of UK Idiopathic Intracranial Hypertension database
- Investigating the role of TGF-β1 in the development of chronic communicating hydrocephalus after subarachnoid haemorrhage: Post-haemorrhagic communicating hydrocephalus is a common complication of intraventricular haemorrhage in premature infants, which often requires permanent ventricular shunting to avert the development of chronic neurological symptoms. We are exploring novel therapeutic strategies to prevent the development of hydrocephalus and improve the outcomes for these infants.
- Neuroendocrine control of brain homeostasis: We are interested in understanding the role that growth factors and other novel peptide hormones may play in CNS homeostasis after trauma. A case of point is a newly recognised neuropeptide encoded by the oesophageal related gene-4 (Ecrg4). Our studies clearly suggest this peptide (augurin) plays a role in CSF homeostasis.

Recent Publications

- Sinclair AJ, Burdon MA, Ball AK, Nightingale NG, Good P, Matthews TD, Jacks A, Lawden M, Clarke CE, Walker EA, Tomlinson J, Stewart PM and Rauz S (2010). **Low energy diet and intracranial pressure in women with idiopathic intracranial hypertension: prospective cohort stud (http://www.ncbi.nlm.nih.gov/pubmed/20610512)** y. *BMJ* 341:c2701
- Sinclair AJ, Walker EA, Burdon MA, van Beek AP, Kema IP, Hughes BA, Murray PI, Nightingale PG, Stewart PM, Rauz S and Tomlinson JW (2010). **Cerebrospinal fluid corticosteroid levels and cortisol metabolism in patients 1 with idiopathic intracranial hypertension: a link between 11β-HSD1 and intracranial pressure regulation (http://www.ncbi.nlm.nih.gov/pubmed/?term=Cerebrospinal+fluid+corticosteroid+levels+and+cortisol+metabolism+in+patients+1+with+idiopathic+intracranial+hypertension%3A+a+link+between+11%CE%B2-HSD1+and+intracranial+pressure+regulation)**? *J Clin Endocrinol Metab* 95(12):5348
- Ball AK, Howman A, Wheatley K, Burdon MA, Matthews T, Jacks AS, Lawden M, Sivaguru A, Furmston A, Howell S, Sharrack B, Davies MB, Sinclair AJ and Clarke CE (2011). **A randomised controlled trial of treatment for idiopathic intracranial hypertension (http://www.ncbi.nlm.nih.gov/pubmed/21161260)**. *J Neurol* 258(5):874
- Gonzalez, AM, Podvin S, Lin SY, Miller MC, Botfield H, Leadbeater WE, Roberton A, Dang A, Knowling SE, Cardenas-Galindo E, Donahue JE, Stopa EG, Johanson CE, Coimbra R, Eliceiri BP and Baird A (2011) **Ecrg4 expression and its product augurin in the choroid plexus: impact on fetal brain development, cerebrospinal fluid homeostasis and neuroprogenitor cell response to CNS injury (http://www.ncbi.nlm.nih.gov/pubmed/?term=Ecrg4+expression+and+its+product+augurin+in+the+choroid+plexus%3A+impact+on+fetal+brain+development%2C+cerebrospinal+fluid+homeostasis+and+neuroprogenitor+cell+response+to+CNS+injury**. *Fluids Barriers CNS* 8(1):6
- Podvin S, Gonzalez AM, Miller MC, Dang X, Botfield H, Donahue JE, Kurabi A, Boissaud-Cooke M, Rossi R, Leadbeater WE, Johanson CE, Coimbra R, Stopa EG, Eliceiri BP and Baird A (2011) **Esophageal cancer related gene-4 is a choroid plexus-derived injury response gene: evidence for a biphasic response in early and late brain injury (http://www.ncbi.nlm.nih.gov/pubmed/?term=Esophageal+cancer+related+gene-4+is+a+choroid+plexus-derived+injury+response+gene%3A+evidence+for+a+biphasic+response+in+early+and+late+brain+injury)**. *PLoS One* 6(9):e24609
- Botfield H, Gonzalez AM, Abdullah O, Skjolding AD, Berry M, McAllister JP 2nd and Logan A (2013) **Decorin prevents the development of juvenile communicating hydrocephalus (http://www.ncbi.nlm.nih.gov/pubmed/?term=Decorin+prevents+the+development+of+juvenile+communicating+hydrocephalus)**. *Brain* 136(Pt 9):2842-58

Staff

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Funding bodies

- **Biotechnology and Biological Sciences Research Council (http://www.bbsrc.ac.uk)**
- **Medical Research Council (http://www.hqip.org.uk)**
- **Healthcare Quality Improvement Partnership (http://www.hqip.org.uk)**
- **National Institute for Health Research (http://www.nihr.ac.uk)**

- **The Midland Neurosciences Teaching and Research Fund (https://sites.google.com/site/mntrfund/projects)**

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