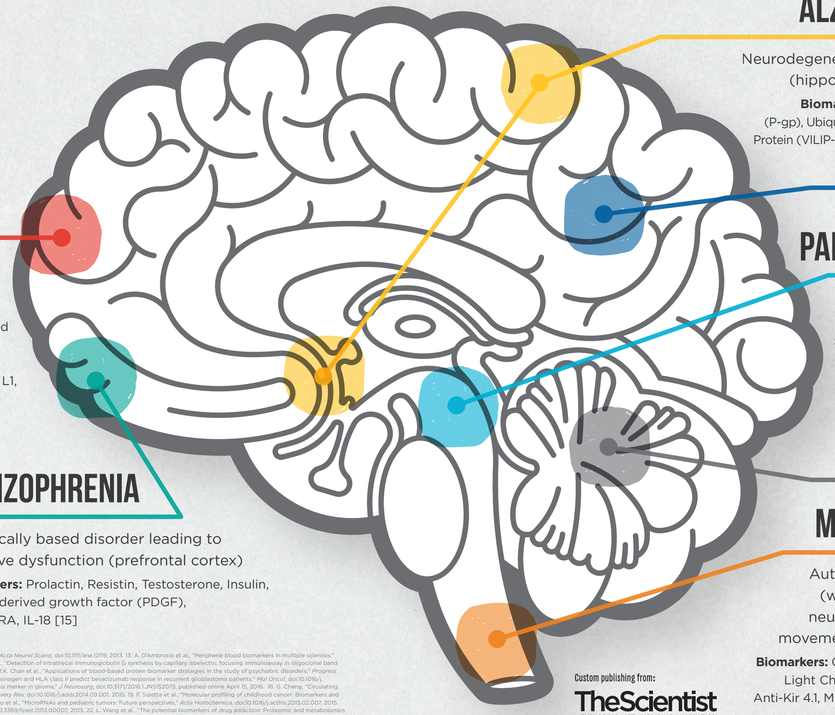
Diagnosing Disease

EXPLOITING BIOMARKERS TO IDENTIFY & MONITOR BRAIN DYSFUNCTION

The central nervous system (CNS) is exquisitely tuned for performing its many core functions, but disease and dysfunction can impede its work. Disease biomarkers are chemical signatures of pathologic processes, detection of which enables diagnosis and progression analysis from blood, cerebrospinal fluid, or tissue biopsy. Biomarkers of CNS disorders have been successfully exploited for their diagnostic and prognostic value, becoming ever more valuable in the fight against insidious diseases that invade and damage our most essential organ system.



TRAUMATIC BRAIN INJURY

Concussive forces lead to swelling, axonal injury, and neurodegeneration (cortex)

Biomarkers: Tau and its phosphorylated states, GFAP, S100β, Neuron-specific Enolase, Chitinase 3-like-1, Ubiquitin Carboxyl-terminal Hydrolase Enzyme L1, IL-1beta, TNF-alpha, IL-6 [8, 9, 10, 11]

DRUG ADDICTION

A physical, psychological, and behavioral need for an exogenous chemical (global)

Biomarkers: Heat-shock protein 70, Peroxiredoxin-6, n-Methylserotonin [22]

SCHIZOPHRENIA

Biologically based disorder leading to cognitive dysfunction (prefrontal cortex)

Biomarkers: Prolactin, Resistin, Testosterone, Insulin, Platelet-derived growth factor (PDGF), IL-8, IL-1RA, IL-18 [15]

ALZHEIMER'S DISEASE

Neurodegeneration leads to memory deficits (hippocampus) and dementia (cortex)

Biomarkers: Tau, Amyloid-β 42, P-glycoprotein (P-gp), Ubiquitin, Apolipoprotein E (ApoE), Visinin-like Protein (VILIP-1), Chitinase 3-like-1 (YKL-40), microRNAs [1, 2, 3, 4]

PARKINSON'S DISEASE

Neurodegeneration in the brain stem (locus coeruleus and substantia nigra) lead to tremor, instability, and dementia

Biomarkers: DJ-1, Synapsin 1 (Syn 1), phosphorylated Syn 1, α-Synuclein, β-Glucocerebrosidase, Uric acid [5, 6, 7*]

MULTIPLE SCLEROSIS

Autoimmune degradation of myelin (white matter) leads to secondary neurodegeneration and progressive movement disorder, leading to paralysis

Biomarkers: Oligoclonal Bands (IgG/M), Kappa Free Light Chains, microRNAs, CXXL13, MOG-IgG & Anti-Kir 4.1, Microtubule-associated protein 2 (MAP2) [12, 13, 14]

GLIOBLASTOMA MULTIFORME

Rapidly progressive, astrocyte-derived brain tumor (cerebral hemispheres)

Biomarkers: Angiotensinogen, HLA Class II, Alpha cardiac muscle 1 (ACTC1), microRNAs [16, 17, 18]

MEDULLOBLASTOMA

High-grade brain tumor with mixed cell types (cerebellum)

Biomarkers: ERBB2, microRNAs, Follistatin-like Protein 5 (FSTL5), miR-495, Prostaglandin D2 Synthase (PGD2S), Polysialylated-Neural Cell Adhesion Molecule (PSA-NCAM) [19, 20, 21]

1. K. Henriksen et al., "The future of blood-based biomarkers for *Alzheimer's disease*," Alzheimer's & Dementia, doi:10.1016/j.jalz.2013.01.013, 2014. 2. A. Hartz et al., "Aβ40 reduces P-glycoprotein at the blood-brain barrier through the ubiquitin-proteasome pathway," *J Neurosci*, doi:10.1523/JNEUROSCI.0350-15.2016, 2016. 3. M.I. Kester et al., "Cerebrospinal fluid VILIP-1 and YKL-40, candidate biomarkers to diagnose, predict and monitor *Alzheimer's disease* in a memory clinic cohort," *Alzheimer's Research & Therapy*, doi:10.1186/s13195-015-0142-1, 2015. 4. W. Gou et al., "Emergence of exosomal miRNAs as a diagnostic biomarker for *Alzheimer's disease*," *J Neurol Sci*, doi:10.1016/j.jns.2015.12.005, 2016. 5. C-H. Lin et al., "Biomarkers of cognitive decline in Parkinson's disease," *Parkinsonism Relat Disord*, doi:10.1016/j.parkreldis.2015.02.010, 2015. 6. L.V. Kalia et al., "Parkinson's disease," *Lancet*, doi:10.1016/S0140-6736(14)61393-3, 2015. 7. G. Esposito et al., "Synaptic vesicle trafficking and Parkinson's Disease," *Developmental Neurobiology*, doi:10.1002/dneu.20969, 2012. 8. K. Kawata et al., "Blood biomarkers for brain injury: What are we measuring?," *Neurosci Biobehav Rev*, doi:10.1016/j.neubiorev.2016.05.009, 2016. 9. C.A. Wiley et al., "Role for mammalian chitinase 3-like protein 1 in traumatic brain injury," *Neuropathology*, doi:10.1111/neup.12158, 2015. 10. J. Li et al., "Serum ubiquitin C-terminal hydrolase L1 as a biomarker for traumatic brain injury: a systematic review and meta-analysis," *Am J Emerg Med*, doi:10.1016/j.ajem.2015.05.023, 2015. 11. J. Zhang et al., "Biomarkers of Traumatic Brain Injury and Relationship to Pathology," *Translational Research in Traumatic Brain Injury*, D. Laskowitz, G. Grant, eds., Boca Raton, Florida: CRC Press/Taylor and Francis Group, 2016, Chapter 12, 2016. 12. R. Dobson et al., "Cerebrospinal fluid and urinary biomarkers in multiple sclerosis," *Acta Neurol Scand*, doi:10.1111/ane.12119, 2013. 13. A. D'Ambrosio et al., "Peripheral blood biomarkers in multiple sclerosis," *Autoimmunity Rev*, doi:10.1016/j.autrev.2015.07.014, 2015. 14. S. Hallegbauer et al., "Detection of intrathecal immunoglobulin G synthesis by capillary isoelectric focusing immunoassay in oligoclonal band negative multiple sclerosis," *J Neurol*, doi:10.1007/s00415-016-8094-3, 2016. 15. M.K. Chan et al., "Applications of blood-based protein biomarker strategies in the study of psychiatric disorders," *Progress Neurobiol*, doi:10.1016/j.pneurobio.2014.08.002, 2014. 16. T. Urup et al., "Angiotensinogen and HLA class II predict bevacizumab response in recurrent glioblastoma patients," *Mol Oncol*, doi:10.1016/j.molonc.2016.05.005, 2016. 17. S. Ohtaki et al., "ACTC1 as an invasion and prognosis marker in glioma," *J Neurosurg*, doi:10.3171/2016.1.JNS152075, published online April 15, 2016. 18. G. Cheng, "Circulating miRNAs: Roles in cancer diagnosis, prognosis, and therapy," *Advanced Drug Delivery Rev*, doi:10.1016/j.addr.2014.09.001, 2015. 19. F. Saietta et al., "Molecular profiling of childhood cancer: Biomarkers and novel therapies," *BBA Clinical*, doi:10.1016/j.bbacli.2014.06.003, 2014. 20. R. Gulino et al., "MicroRNAs and pediatric tumors: Future perspectives," *Acta Histochemica*, doi:10.1016/j.acthis.2015.02.007, 2015. 21. M.D. Russell et al., "Biomarkers of pediatric brain tumors," *Front Pediatr*, doi:10.3389/fped.2013.00007, 2013. 22. L. Wang et al., "The potential biomarkers of drug addiction: Proteomic and metabolomics challenges," *Biomarkers*, doi:10.1080/1354750X.2016.1201530, 2016.

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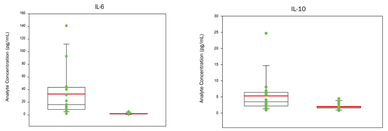
Ella pinpoints new brain injury biomarkers

Not a lot of sample? Low-level proteins? Ella doesn't mind.

In many disease states, low-level proteins are hard to detect with any consistency. For a group of chemokines linked to Traumatic Brain Injury (TBI), Ella makes that task easy.

When neuroinflammatory biomarkers are released from neurons post-brain injury, their presence can negatively affect brain function by increasing cytokine levels that lead to neural damage. To provide a more complete picture of the TBI process, Mike Anderson and colleagues at R&D Systems evaluated multiple neuroinflammatory markers using Simple Plex™ multi-analyte ELISAs run on Ella.

Simple Plex™ easily confirmed low levels quantitatively, because the assay format is that robust. So even if you have several researchers using the assay, or your sample pipetting varies, Ella will still provide you with quantitative and reproducible results, at picogram/mL levels.



Proteins that could act as markers for Traumatic Brain Injury. IL-6 and 10 are just two of many analytes with increased concentrations in TBI samples compared to control samples.

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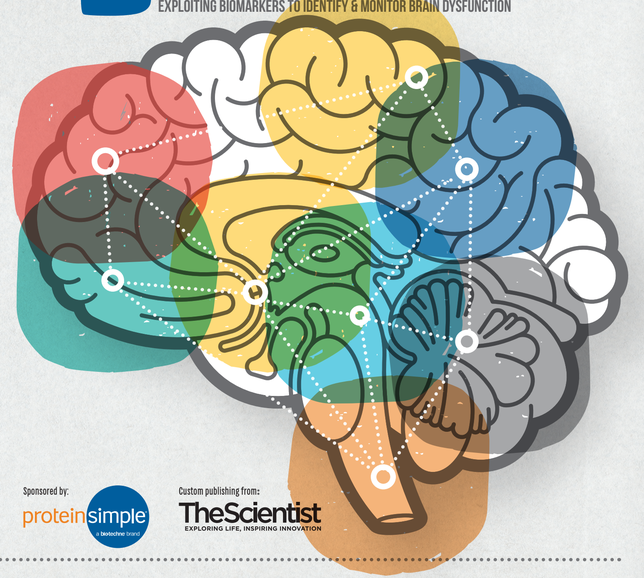

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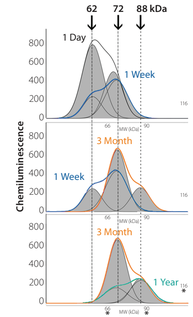
EXPLORING LIFE, INSPIRING INNOVATION

Wes sets a new pace for Alzheimer's research

At the Barshop Institute for Longevity and Aging Studies, University of Texas Health Science Center in San Antonio, researchers study the basic biology of aging. One project in particular focuses on how age-associated changes in normal physiology alter the expression and function of tau, a biomarker for many neurodegenerative disorders, including Alzheimer's disease. Using traditional Western blotting to study the correlation between tau's expression and aging proved to be challenging, particularly with small sample size collected from brain sub-regions.

With Wes, they run 24 independent samples and get fully analyzed data in about 3 hours. All that with 95% less tissue and antibody. Data was reproducible and reliable. Furthermore, they discovered a novel high molecular weight isoform of tau protein that is expressed in the brains of the naked mole-rat (NMR). The results showed that tau undergoes a progressive shift in molecular weight during the first year of NMR brain development (M.E. Orr et al., Neurobiology of Aging, 36, 2015).

Don't let old technologies slow down your research. Win the race to discovery with Wes.



Detection of tau in nakedmole rats (NMR) in different stages of life development using Wes. A progressive molecular weight shift in NMR tau is observed during development. (HT7 antibody recognizes tau at an epitope corresponding to human tau 159-163).

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