Trainee to Faculty

Reflections on my CTMC time

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CTMC Class of 2017

Most Memorable Lesson Learned

Cringe-Worthy

- **3a. Please state in one sentence what the main goal of the current clinical trial or study will be**: The goal is to determine the optimal dose and treatment duration of omega-3 fatty acid treatment in acute mild TBI that are most likely to be efficacious in a phase III clinical trial
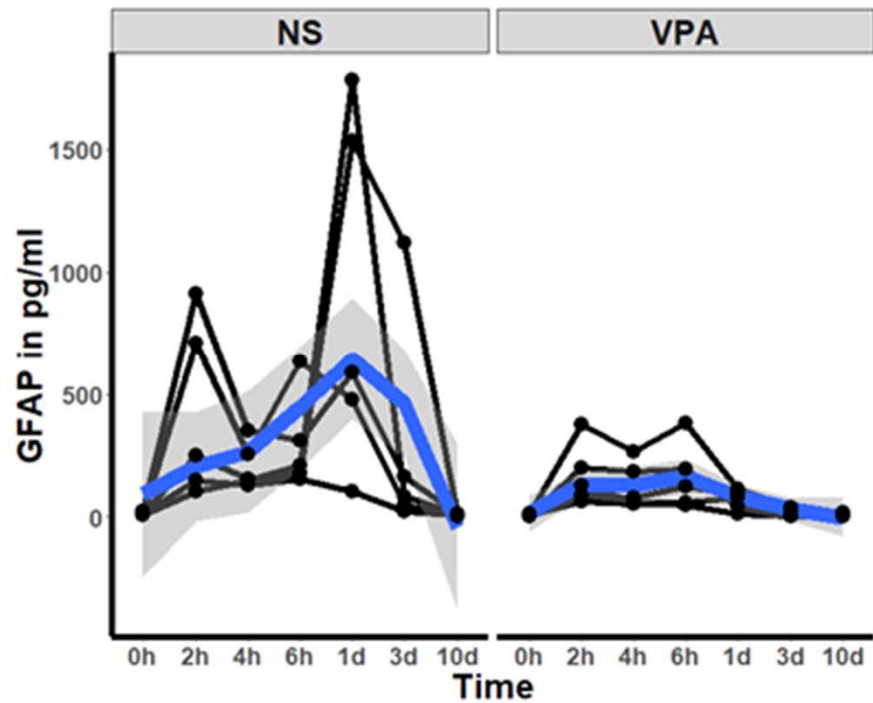
OPTIMA-TBI Pilot

- Pilot Study of Omega-3 Polyunsaturated Fatty Acid Treatment in Mild Acute TBI (OPTIMA-TBI pilot).

- **Objective:** Determine the effect of high dose DHA on neurodegeneration and neuroinflammation post-TBI as measured by blood-based biomarkers

- **Population**: Adult (18-65 years), Head CT negative, GCS 13-15 TBI without significant polytrauma

- **Intervention**: 6g/day DHA+EPA x 1 month + 1.2g/day x 2 months versus placebo

MILD TBI

Head CT negative,
GCS 13 - 15 TBI

Blood-based biomarkers for monitoring response to therapy

OPTIMA-TBI Pilot

- 32 subjects enrolled and randomized to DHA or Olive Oil (placebo)

- Blood samples obtained at enrollment, 2 weeks, 1 month, 3 months

- Neurocognitive tests performed at 2 weeks, 1 month and 3 months

Reflection 1: Don't be afraid of change

Reflection 2: Think carefully about critiques before responding

Which subjects will you enroll in the trial?

How accurate is clinical gestalt?

- 217 ED patients with GCS 13-15 TBI

- Based on what you know now about this patient's presentation, do you think this patient will have a complete functional recovery i.e. they will be back to their pre-TBI functional state at 3 months after injury? (yes/no)

- How certain are you that your prediction will be right? (0-100)

- Based on what you know now about this patient's presentation, do you think this patient will have 3 or more post-concussive symptoms (for example: headaches, fatigue, insomnia, loss of concentration, noise and light sensitivity, memory loss, dizziness) at 3 months after injury? (yes/no)

- How certain are you that your prediction will be right? (0-100)

		Delayed functional Recovery	Delayed Symptom Recovery
Resident/ Midlevel	Sensitivity	5.2%	34.3%
	Specificity	97.1%	84.3%
	Positive Predictive Value	66.7%	67.9%
	Negative Predictive Value	52.4%	43.1%
Attending	Sensitivity	8.1%	54.5%
	Specificity	92.5%	82.5%
	Positive Predictive Value	50.0%	63.2%
	Negative Predictive Value	52.1%	60.0%

Prognostic enrichment based on currently available data

- 372 ED patients with GCS 13-15 TBI

Figure 1: Feature Selection Using Bagged Decision Trees

AUC: 0.888
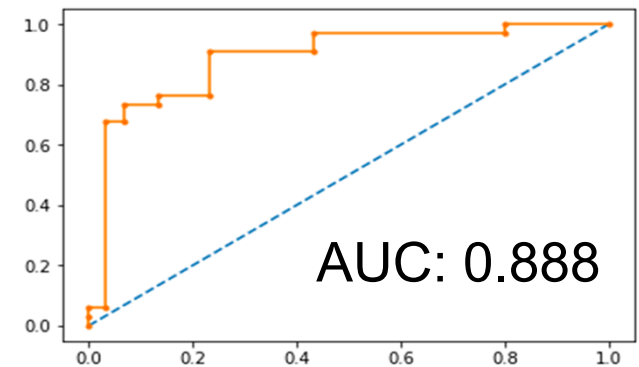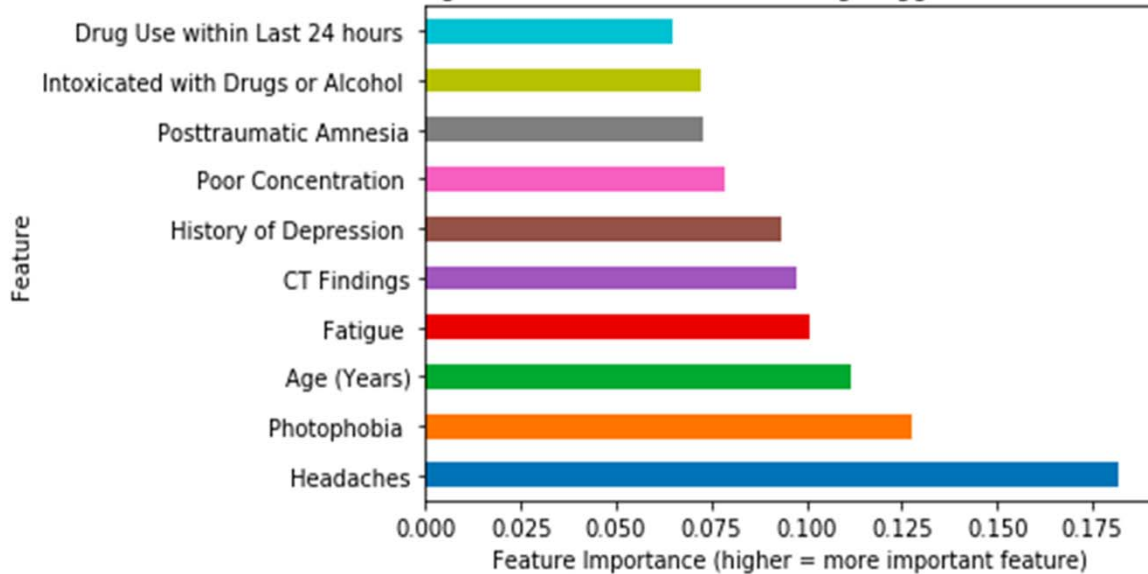
Blood-Based Biomarkers of Brain Injury and TBI

Serum GFAP and UCH-L1 for prediction of absence of intracranial injuries on head CT (ALERT-TBI): a multicentre observational study

Jeffrey J Bazarian*, Peter Biberthaler*, Robert D Welch, Lawrence M Lewis, Pal Barzo, Viktoria Bogner-Flatz, P Gunnar Brolinson, Andras Büki, James Y Chen, Robert H Christenson, Dallas Hack, J Stephen Huff, Sandeep Johar, J Dedrick Jordan, Bernd A Leidel, Tobias Lindner, Elizabeth Ludington, David O Okonkwo, Joseph Ornato, W Frank Peacock, Kara Schmidt, Joseph A Tyndall, Arastoo Vossough, Andy S Jagoda

Summary
Background More than 50 million people worldwide sustain a traumatic brain injury (TBI) annually. Detection of

Lancet Neurol 2018; 17:782–89

Performance Evaluation of a Multiplex Assay for Simultaneous Detection of Four Clinically Relevant Traumatic Brain Injury Biomarkers

Frederick K. Korley,[1,*] John K. Yue,[2,*] David H. Wilson,[3] Kevin Hrusovsky,[3] Ramon Diaz-Arrastia,[4] Adam R. Ferguson,[2] Esther L. Yuh,[5] Pratik Mukherjee,[5] Kevin K. W. Wang,[6] Alex B. Valadka,[7] Ava M. Puccio,[8] David O. Okonkwo,[8] and Geoffrey T. Manley[2]
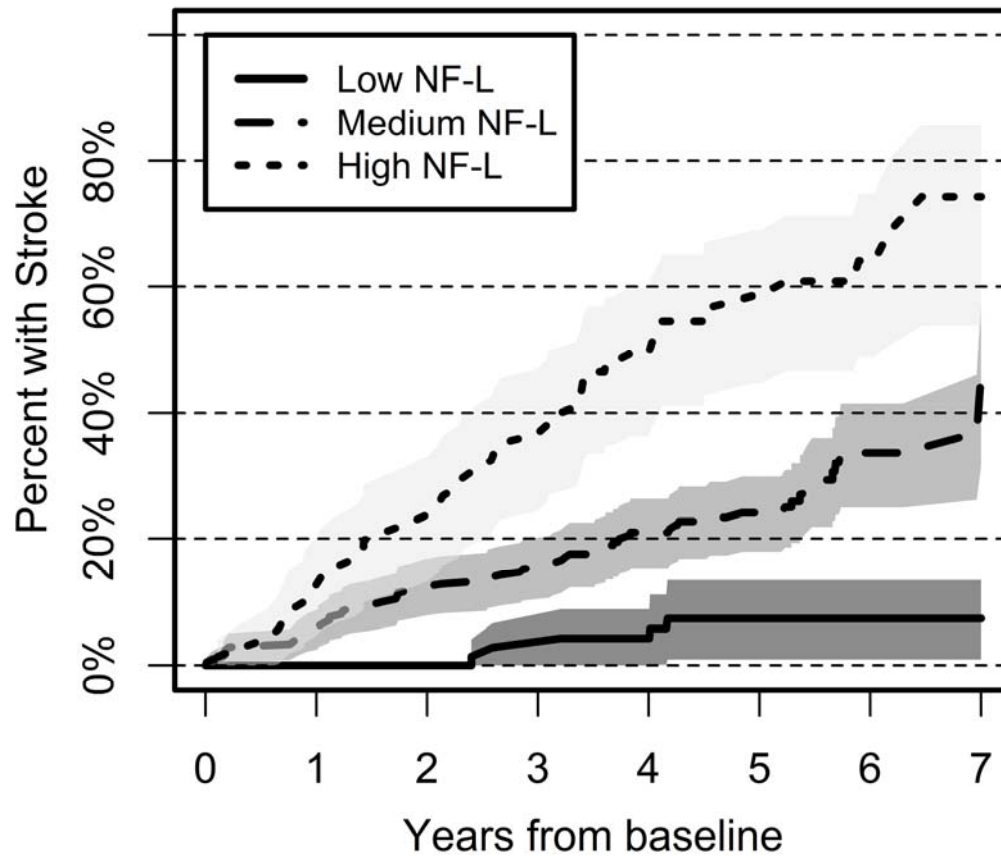
Prognostic enrichment using blood based biomarkers
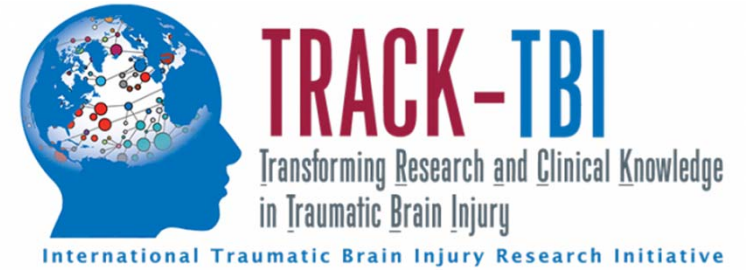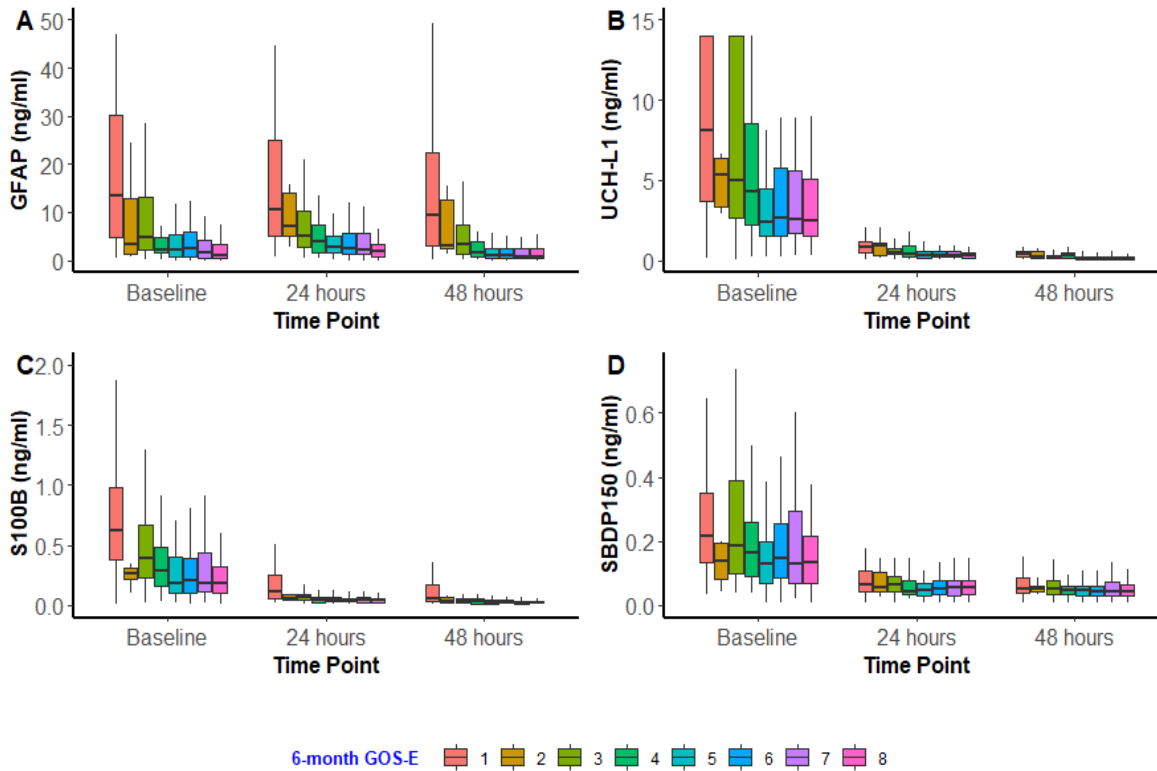
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Bio-ProTECT

Serum NfL levels predict incident stroke in diabetics

Future trial of GCS 13-15 TBI

Reflection 3: Don't give up

Baby Steps

Accomplishments since course

- Co-MPI: NINDS funded Hyperbaric Oxygen in Brain Injury Treatment Trial (HOBIT)

- Co-MPI: DoD Funded Biomarkers in the Brain Oxygen Optimization in TBI Phase III (Bio-BOOST) study

- PI: Biomarkers in the Hyperbaric Oxygen in Brain Injury Treatment Trial (Bio-HOBIT) - reviewed today

- PI: NHLBI funded R21 Predicting Incident Stroke Using Blood Biomarkers of Brain Injury

- Co-I: DoD funded Transforming Research and Clinical Knowledge in TBI Network (TRACK-TBI NET)

- Co-I: NIH funded Strategies to Innovate Emergency Care Clinical Trials Network (SIREN)

LUCK = Preparation + Opportunity

Reflection 4: **Take good care of yourself**