Evidence Update on COVID-19
Biomarkers

This is a summary of the latest evidence available on the treatments being testing *in vitro* and *in vivo* for COVID-19. It is not comprehensive and will be updated as more treatments and data is published.

Cardiac troponin

Troponin is a protein involved in heart muscle contraction. On damage to the heart, troponin is released into the blood. 85% sepsis patients also have elevated troponin Smith

Elevated troponin is seen in severe cases of COVID-19

- Cardiac injury is a possible mechanism contributing to severe illness and mortality
- Review - In China, those with elevated troponin were older, had higher rates of comorbidities including hypertension, CAD and diabetes, were more likely to be admitted to ICU and die Tersalvi
- 341 patient meta analysis - troponin levels increased in severe patients (25.6ng/L) and indicates cardiac damage and predicts worse outcomes (small, variable studies, methodology and timing of measurement unknown) Lippi
- 41 patients - troponin increased in 5 patients with cardiac injury due to virus Huang
- 47 patients in Wuhan - troponin elevated in severe patients on admission Han
- 187 patients in Wuhan - 28% had elevated troponin levels (but 35% had underlying CVD)
  - Mortality was elevated in patients with CVD and high troponin vs CVD and normal troponin (13% vs 70%) (low N for analysis) Guo

D-dimer

D-dimer is a fibrin degradation product, released when a blood clot is broken down. It is usually elevated in patients with thrombosis, and also the elderly with various illnesses Halaby

Elevated D-Dimer in seen in severe cases of COVID-19

- 248 patients - D-dimer elevated in 75% patients and increased with disease severity and death - >2.14mg/L predicted mortality (pre-print) Yao
- 57 patients - D-dimer was was higher in COVID-19 vs. CAP patients, and decreased following treatment (low n, unclear what the levels were) Yu
- 41 patients - ICU patients had increased D-dimer 2.4mg/L vs. 0.5mg/L (4 days post admission, 7 days from onset) Huang
- 47 patients in Wuhan - D-dimer elevated in severe patients on admission Han
- 183 patients - D-dimer 3.5 fold higher in severe (2.12mg/L) then mild (0.61mg/L) COVID-19 Tang
- 138 PATIENTS - D-dimer 2.5 fold higher in severe (4.14mg/L) then mild (1.66mg/L) Wang
- 191 patients - D-dimer 9 fold higher in patients who died (5.2mg/L) then survived (0.6mg/L) Zhou

Lymphopenia

Lymphopenia is a reduced blood lymphocyte count, due to sequestration of lymphocytes to lymph nodes during viral infection Harvey

Lower lymphocyte count appears to predict severity and mortality in COVID-19

- 47 patients in Wuhan - Lymphocyte count below 1.045x109/L identified severe patients Han
- 52 patents - 80% severe patients had lymphocytopenia Yang
- 1099 patients - Lymphocytopenia was present in 83% all admitted COVID-19 patients, but worse in severe patients Guan
- 150 patients - Those that died had lower lymphocyte count (0.6x109/L) vs those discharged (1.42x109/L) - but were also older (62 vs 50) Raun

Blood IL-6

IL-6 is a proinflammatory cytokine that is elevated during infection. It stimulated innate immune cells including neutrophils, and adaptive immune cells including B cells and is elevated in sepsis Tanaka
Elevated IL-6 in severe cases

- High IL-6 levels 80pg/ml associated with mechanical ventilation (median time to MV 1.5 days), 92% risk of respiratory failure - 22 times higher then low IL-6 (40 hospitalised patients, 13 on MV - don't have any info on patients and timing of samples) Herold
- 43 patients - IL-6 increased in severe vs. mild cases 36pg/ml vs. 11pg/ml Gao

LDH - Lactate dehydrogenase

LDH is an enzyme that converts lactate to pyruvate in all cells, and is a marker of tissue damage
Smith
Elevated LDH in severe cases

- 47 patients in Wuhan - serum LDH above 283U/l identified severe patients and correlated with clinical severity, APACHE II and SOFA scores (long term follow up not available) Han
- 120 patients - Severe patients had high LDH (70% had > 250U/L, OR 2.5) Zhang

Fibrinogen

Fibrinogen is a glycoprotein that is converted to fibrin and forms a blood clot. Is it also an acute phase protein and is elevated in infection Hayakawa
Elevated fibrinogen in severe cases

- 22 patients with severe COVID-19 - elevated fibrinogen 517 vs 297mg/dL in 44 healthy controls (but controls were not in ICU - doesn't tell us much) Spiezia
- 69 patients - fibrinogen increased in severe cases (unclear analysis of severity) Wang
- 43 patients - fibrinogen increased in severe 3.84 vs. 3.11 g/L severe vs. mild covid - predictor for severity Gao

Serum Amyloid A

SAA is an acute phase protein released by hepatocytes that stimulates immune cell chemotaxis and has antimicrobial effects. Todorov

- 132 patients - SAA and CRP increased in COVID-19 patients (no control group), and correlated with disease progression. High SAA on admission had poorer CT scans Li