

- Circulating mesothelial precursor cells -

A new opportunity to detect pleural damage and mesothelioma

after asbestos exposure?

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Conflict of interest

- Bayer (speaker fees)
- Astra-Zeneca (Ad board)

Acknowledgement



Bill Duong
(Shana Kelley's lab)

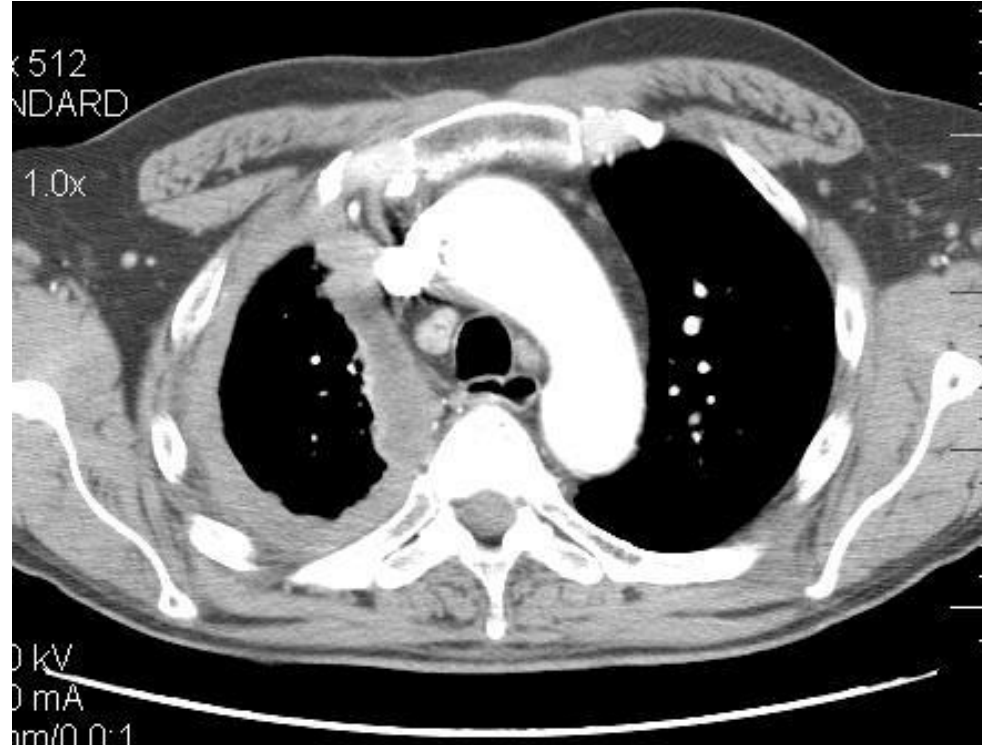


Licun Wu

Work in progress

Mesothelioma characteristics

- Rapid progression
- Late diagnosis
- Invasion of local structures (heart, chest wall)
- Symptoms are
 - Chest pain
 - Shortness of breath
 - Weight loss
 - Fatigue



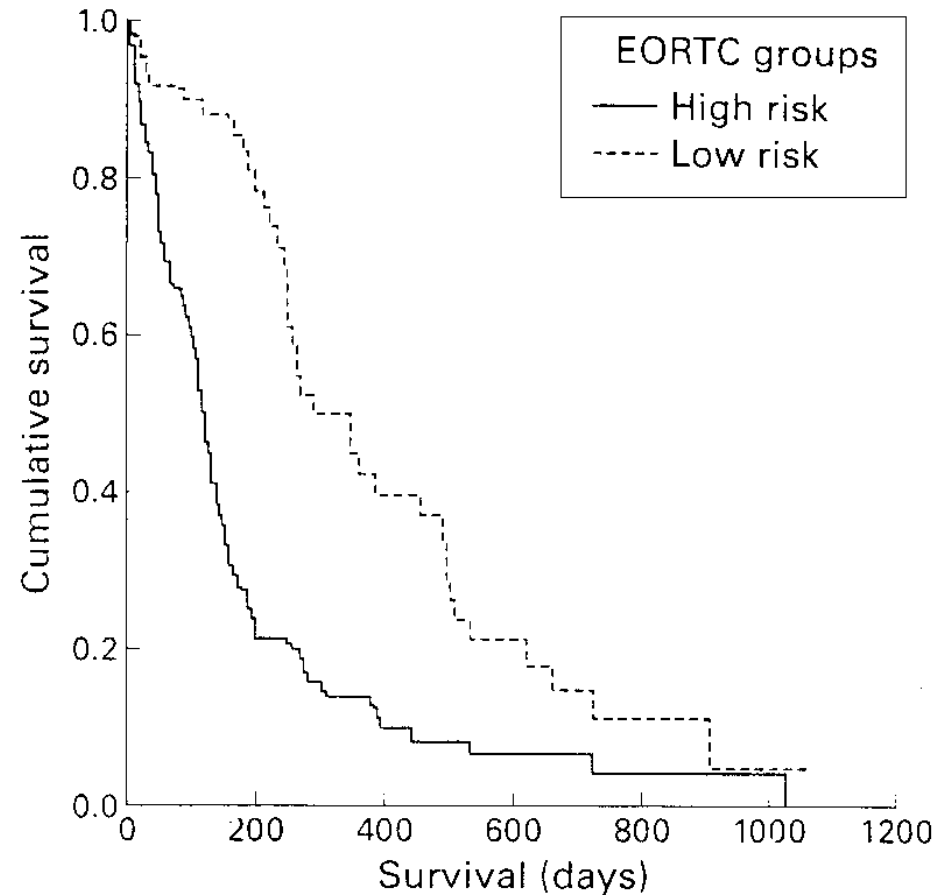
Outcome of mesothelioma after diagnosis

Median survival

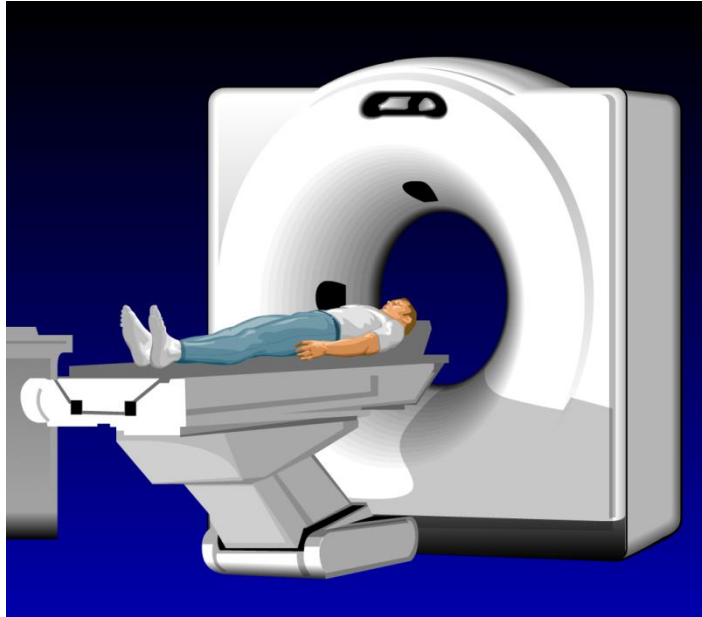
- 6 - 12 months

Prognostic factors

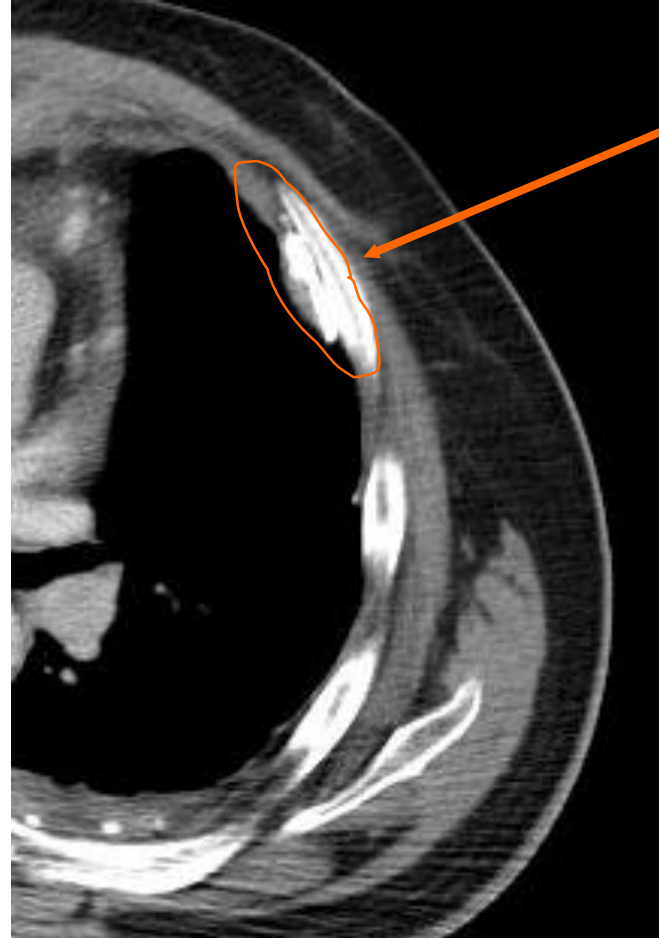
- Performance status
- Histology
- Gender
- Inflammatory markers (CRP, WBC, platelets, fibrinogen)



Screening program is active since 2005 in Toronto



Low dose CT chest for patients with history of asbestos exposure or pleural plaques



Characterize plaques at risk of transformation to mesothelioma

Screening program

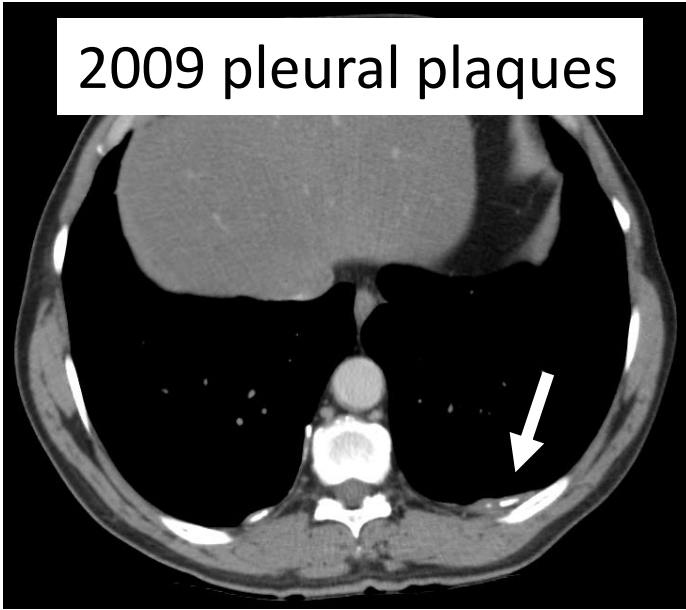
- 2005 - 2019
- Enrolled about 1,500 individuals
- Previous asbestos exposure or presence of pleural plaques
- Median age of participants is 61 yo (32-85 yo)
- Smoking history: 73% of participants
- Blood sample collected at each visit

Number of cancer detected

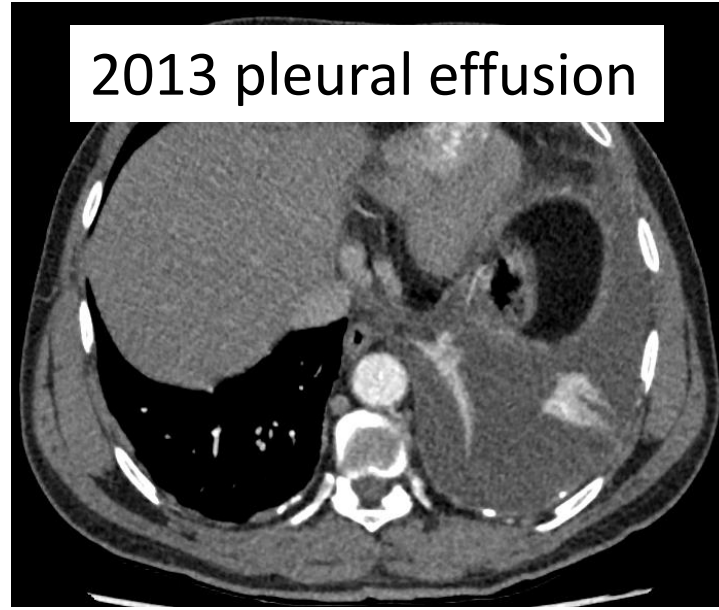
Number of participants	1156
Total number of thoracic malignancies	16
Lung cancer	8
Pleural mesothelioma	4
Abdominal mesothelioma	4

Mesothelioma in situ (BAP1 lost with no invasion on histology)

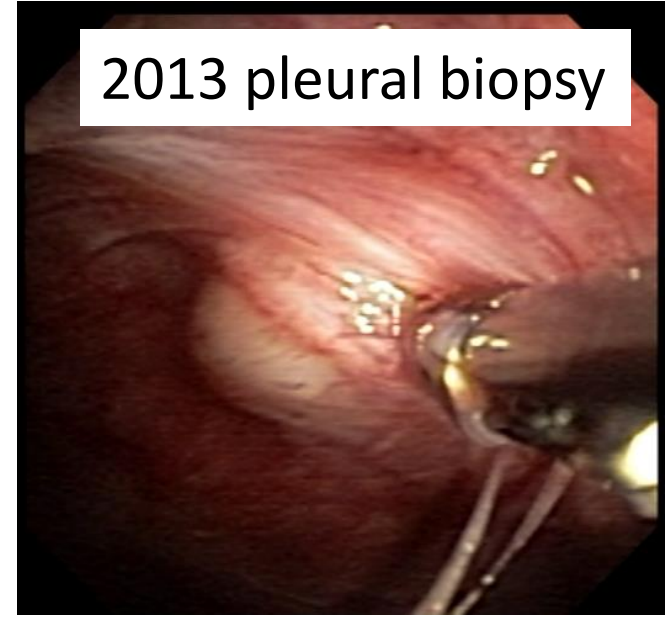
2009 pleural plaques



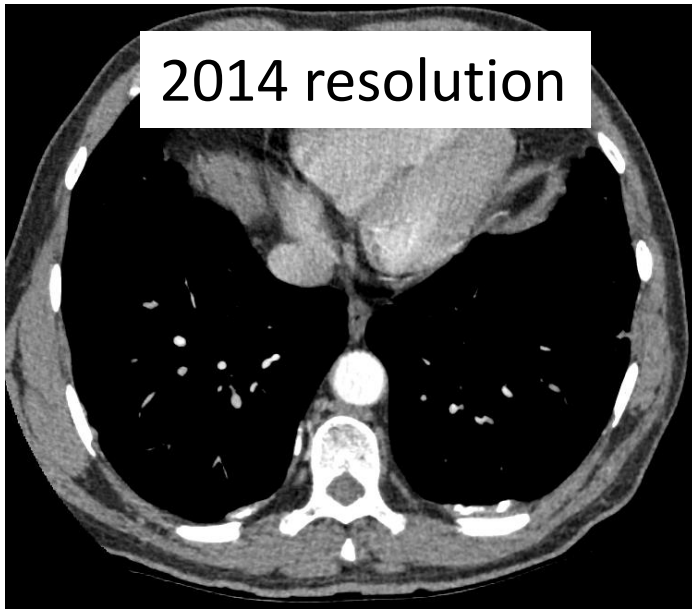
2013 pleural effusion



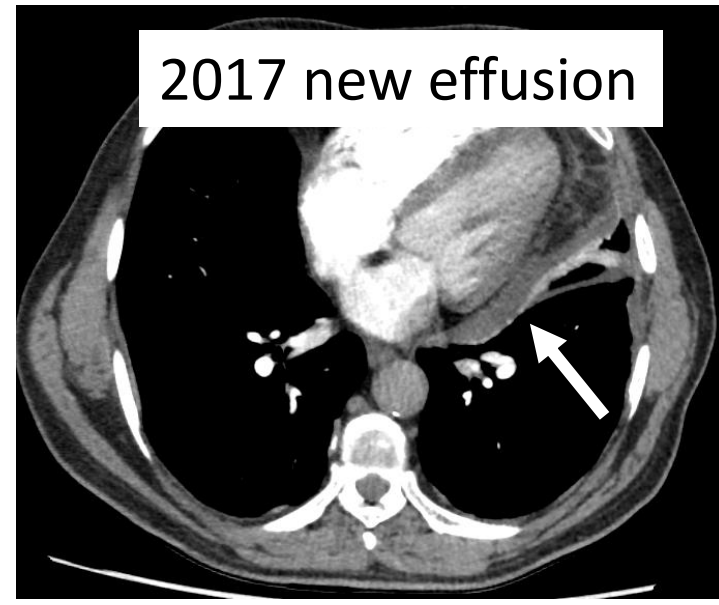
2013 pleural biopsy



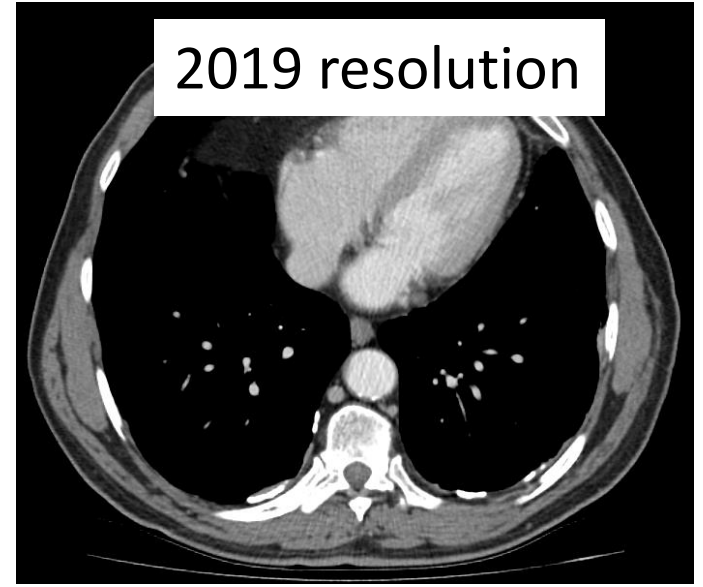
2014 resolution



2017 new effusion

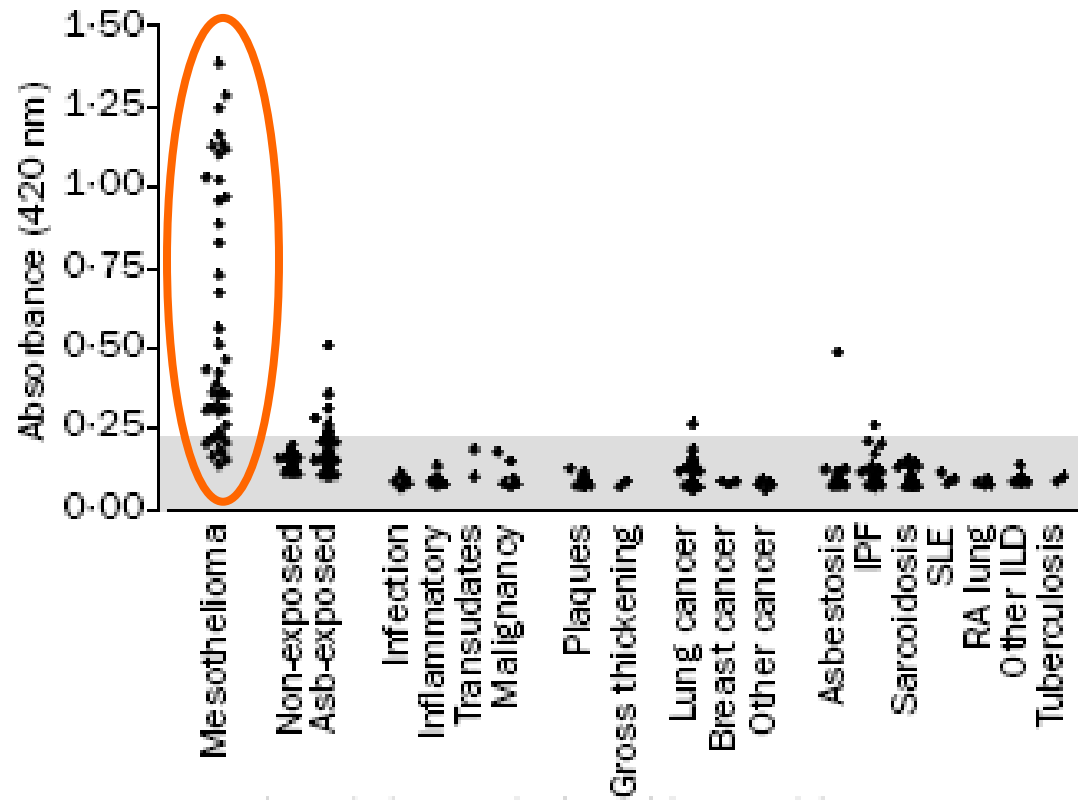


2019 resolution



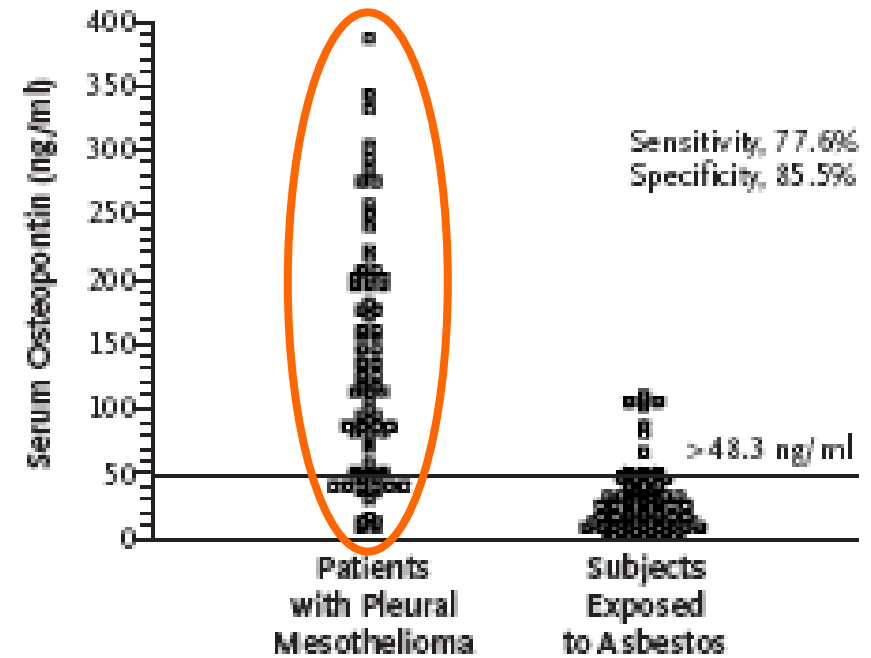
Role of serum markers for early detection

Mesothelin



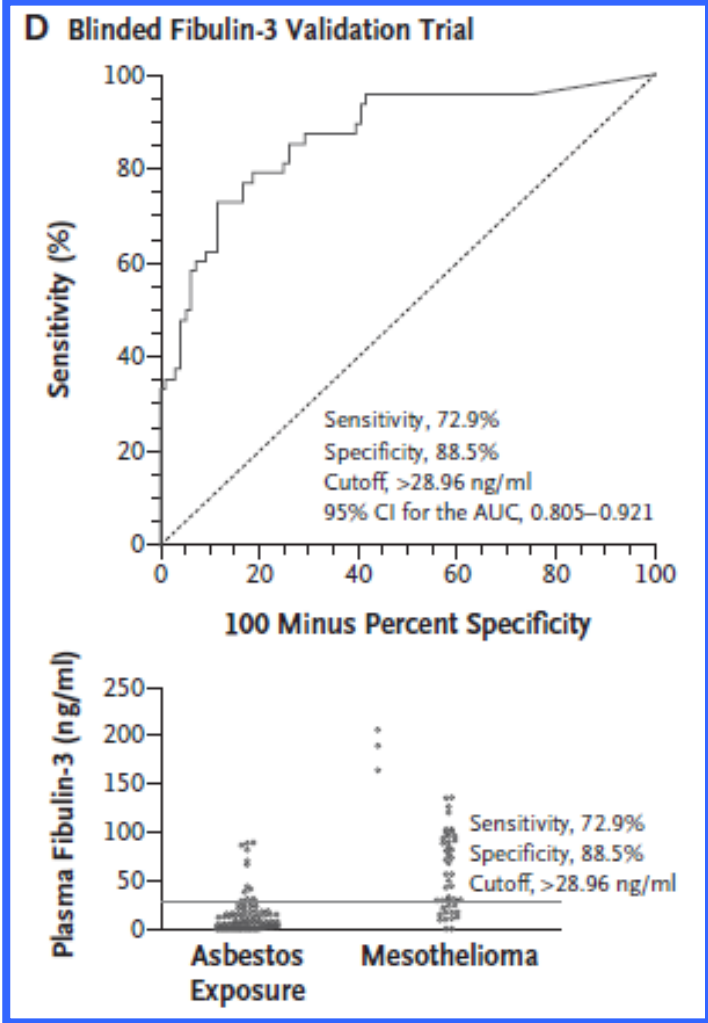
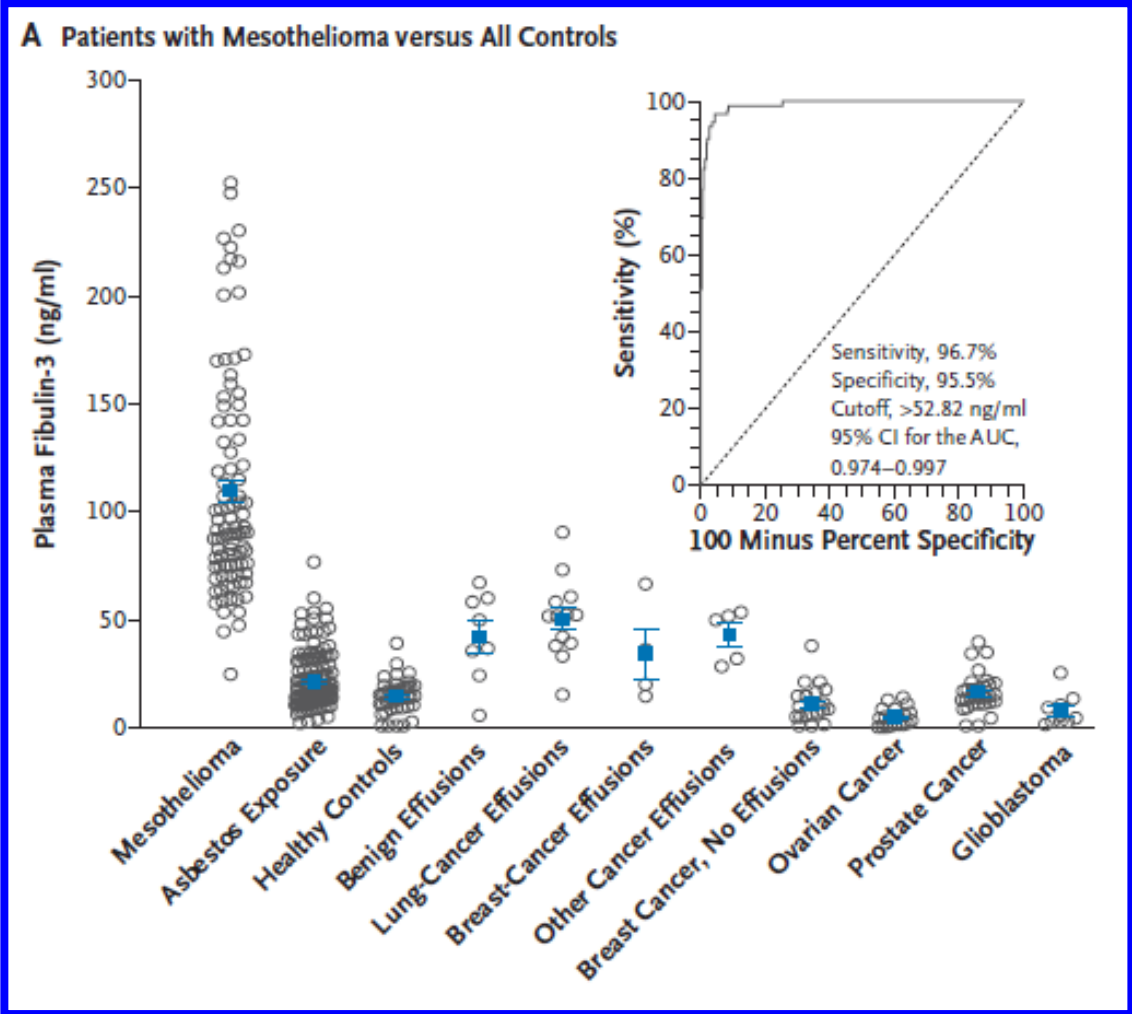
Lancet 2003;362:1612-16

Osteopontin



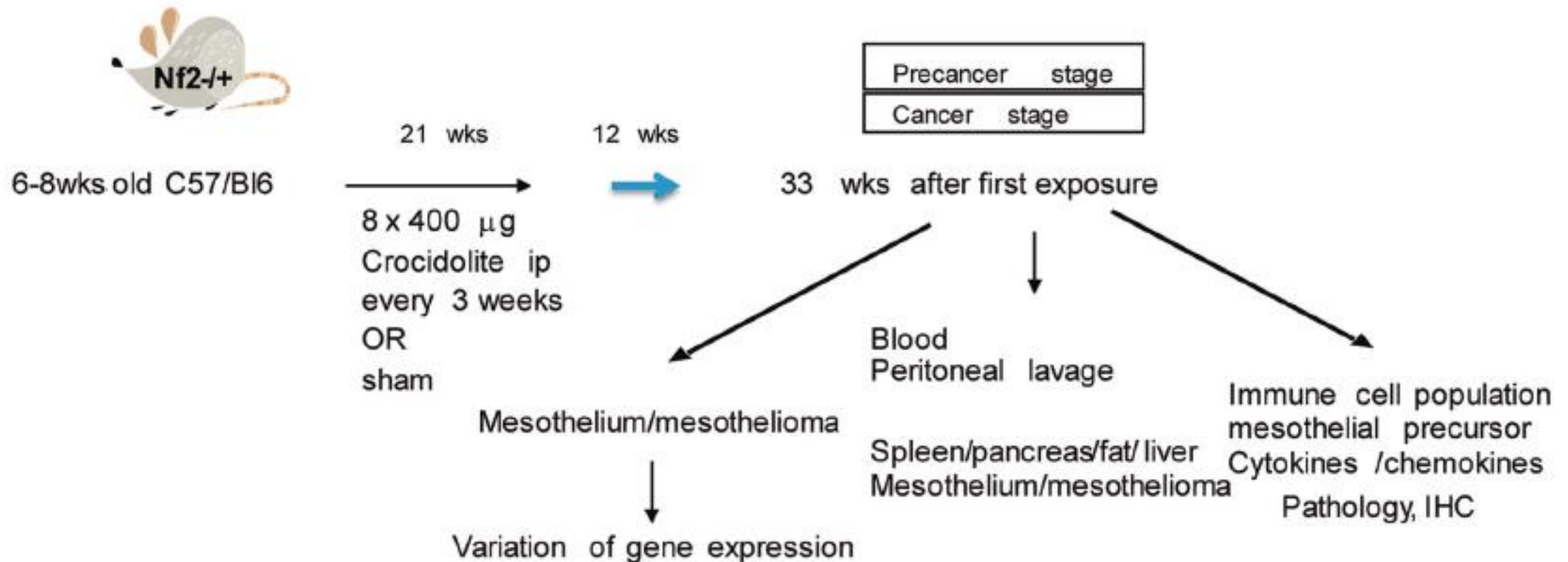
NEJM 2005;353:1564-73

Fibulin-3 in mesothelioma



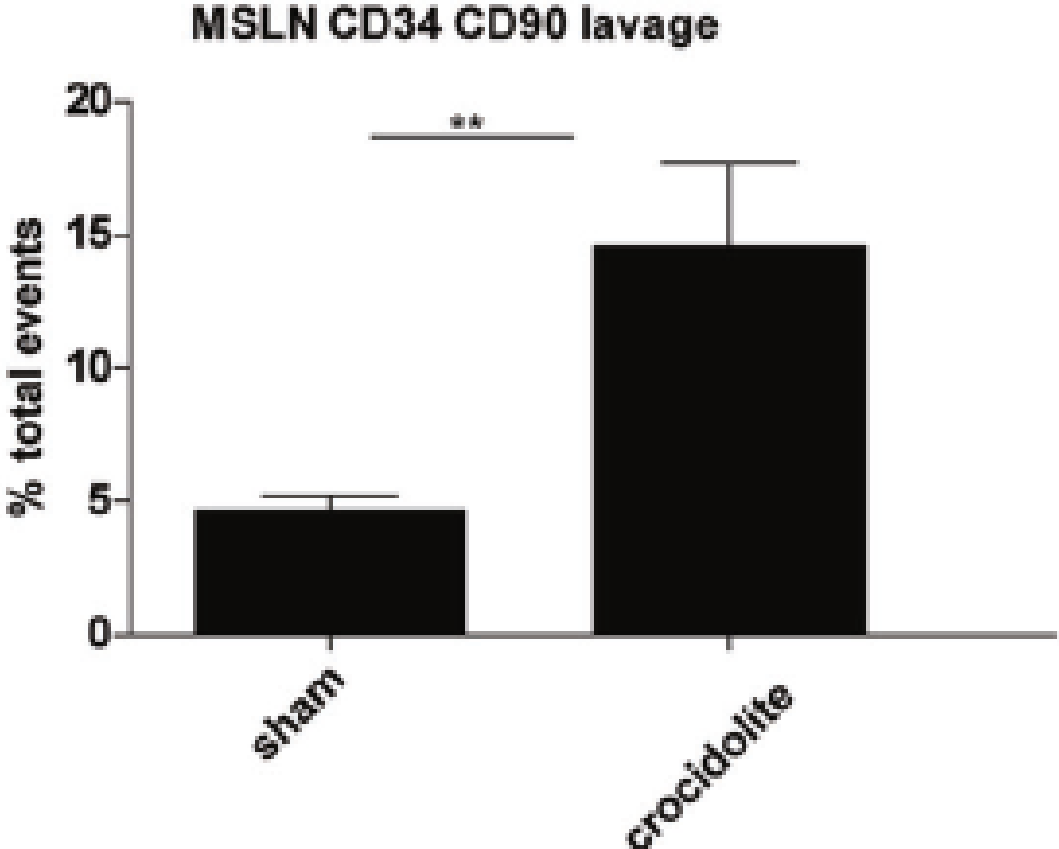
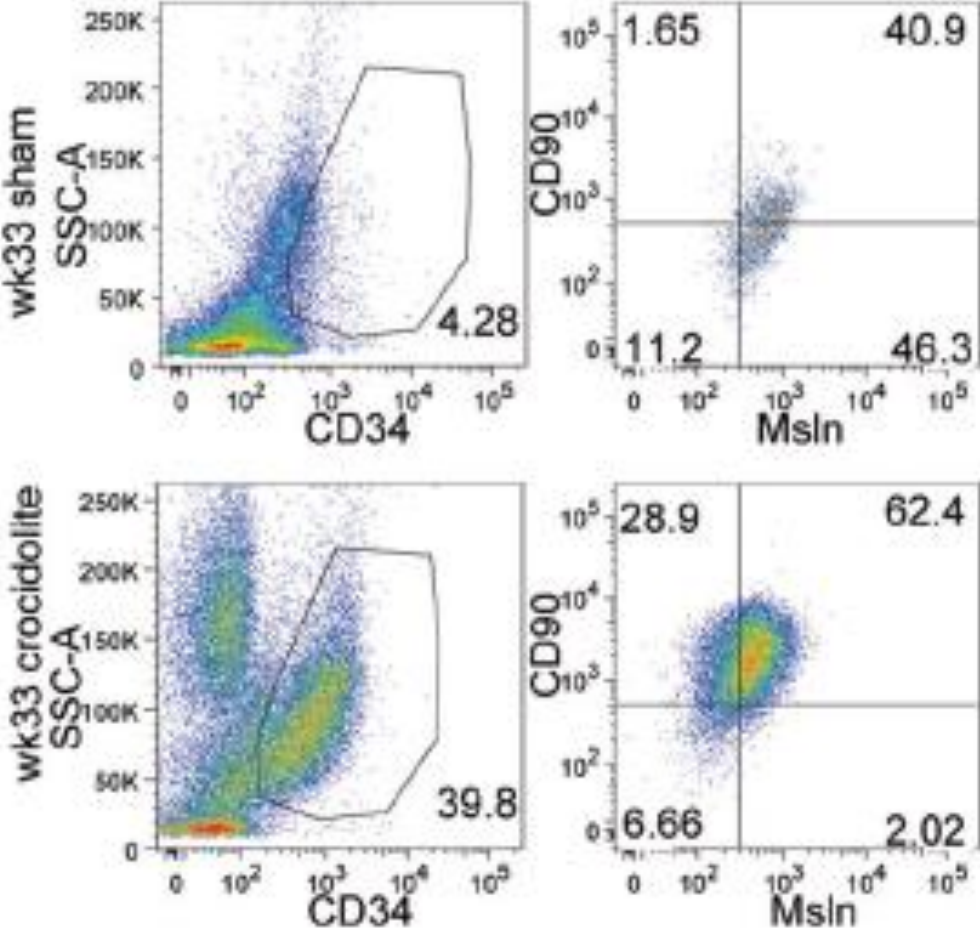
How asbestos drives the tissue towards tumors: YAP activation, macrophage and mesothelial precursor recruitment, RNA editing, and somatic mutations

Hubert Rehrauer¹ · Licun Wu² · Walter Blum³ · Lazslo Pecze³ · Thomas Henzi³ · Véronique Serre-Beinier⁴ · Catherine Aquino¹ · Bart Vrugt⁵ · Marc de Perrot² · Beat Schwaller³ · Emanuela Felley-Bosco⁶



Peritoneal lavage after asbestos exposure

Mesothelial progenitor cells



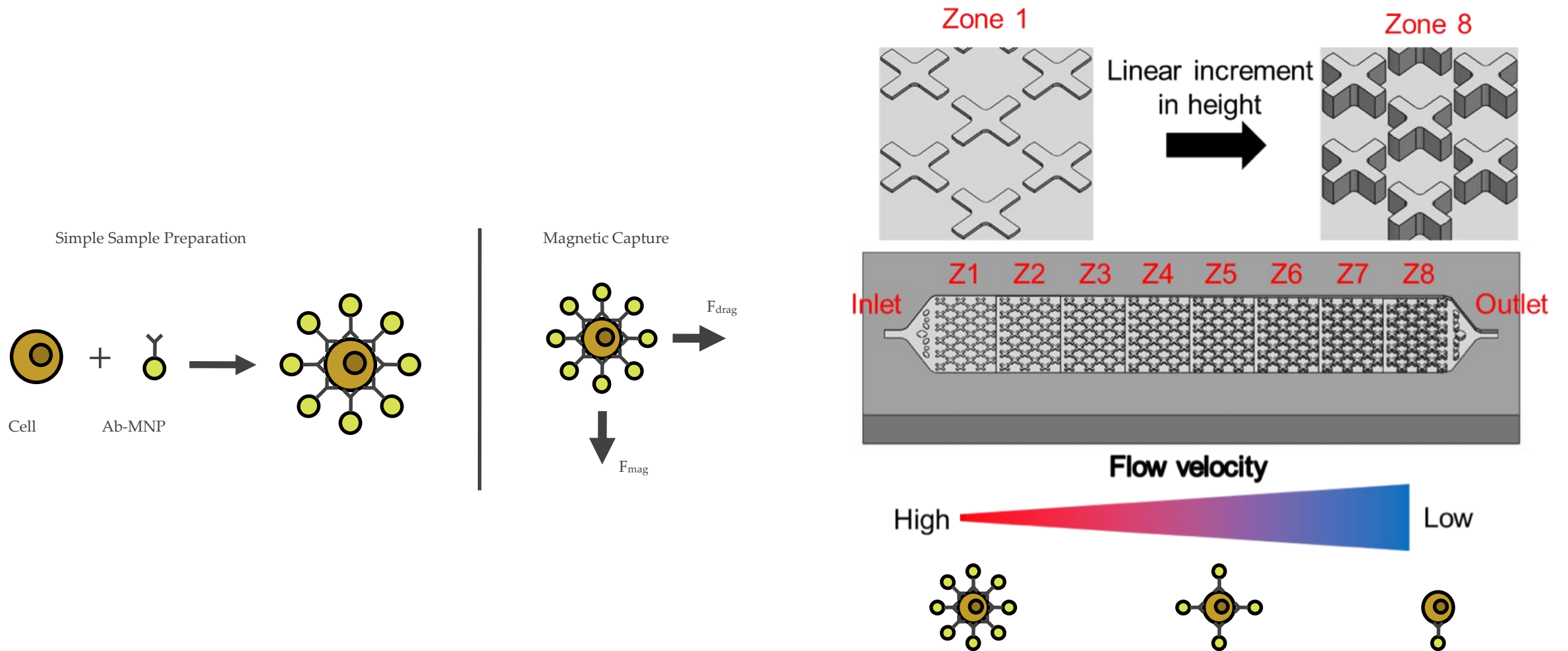
Tracking the dynamics of circulating tumour cell phenotypes using nanoparticle-mediated magnetic ranking

Mahla Poudineh¹, Peter M. Aldridge², Sharif Ahmed³, Brenda J. Green², Leyla Kermanshah², Vivian Nguyen³, Carmen Tu³, Reza M. Mohamadi³, Robert K. Nam⁴, Aaron Hansen⁵, Srikala S. Sridhar⁵, Antonio Finelli⁵, Neil E. Fleshner⁵, Anthony M. Joshua⁵, Edward H. Sargent^{1*} and Shana O. Kelley^{2,3,6*}

Magnetic ranking cytometry

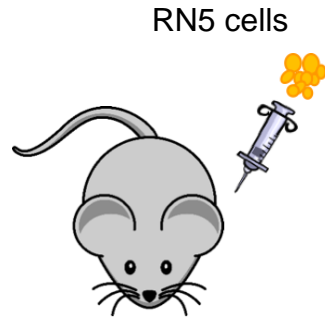
- New approach that leverage immunomagnetic separation for profiling circulating cells based on their cell surface markers
- Whole blood sample is incubated with antibody-functionalized magnetic nanoparticles
- Phenotypic profile at a single cell level
- Very high level of sensitivity with the ability to profile cells at very low level of 10 cell per ml of blood

zxViva Device Overview



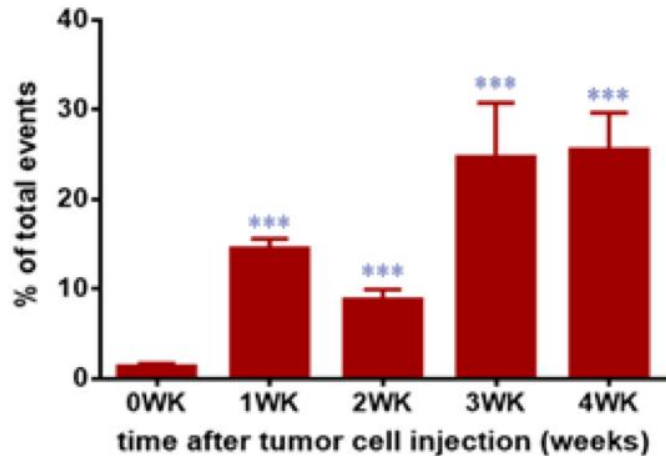
Courtesy of Bill Duong and Shana Kelley

Intraperitoneal mesothelioma model (x 6 weeks)



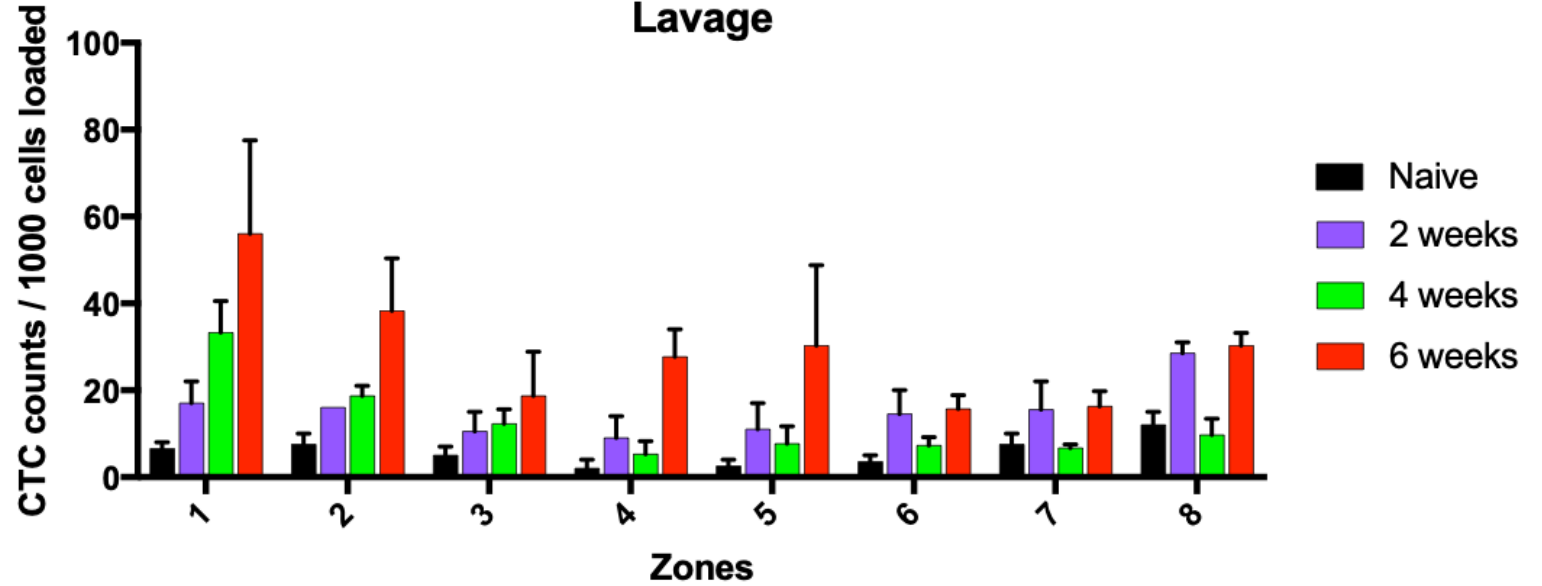
Flow cytometry of peritoneal lavage

MSLN+CD34+CD90+ in lavage

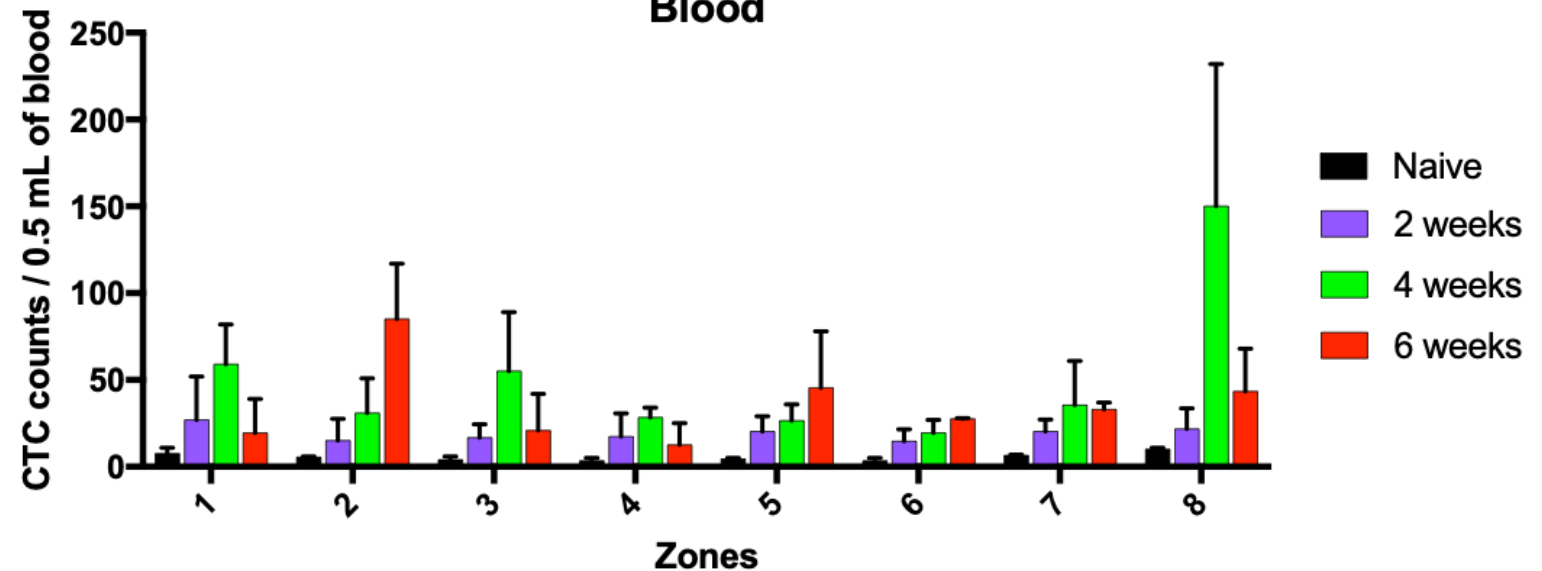


Magnetic ranking cytometry

Lavage

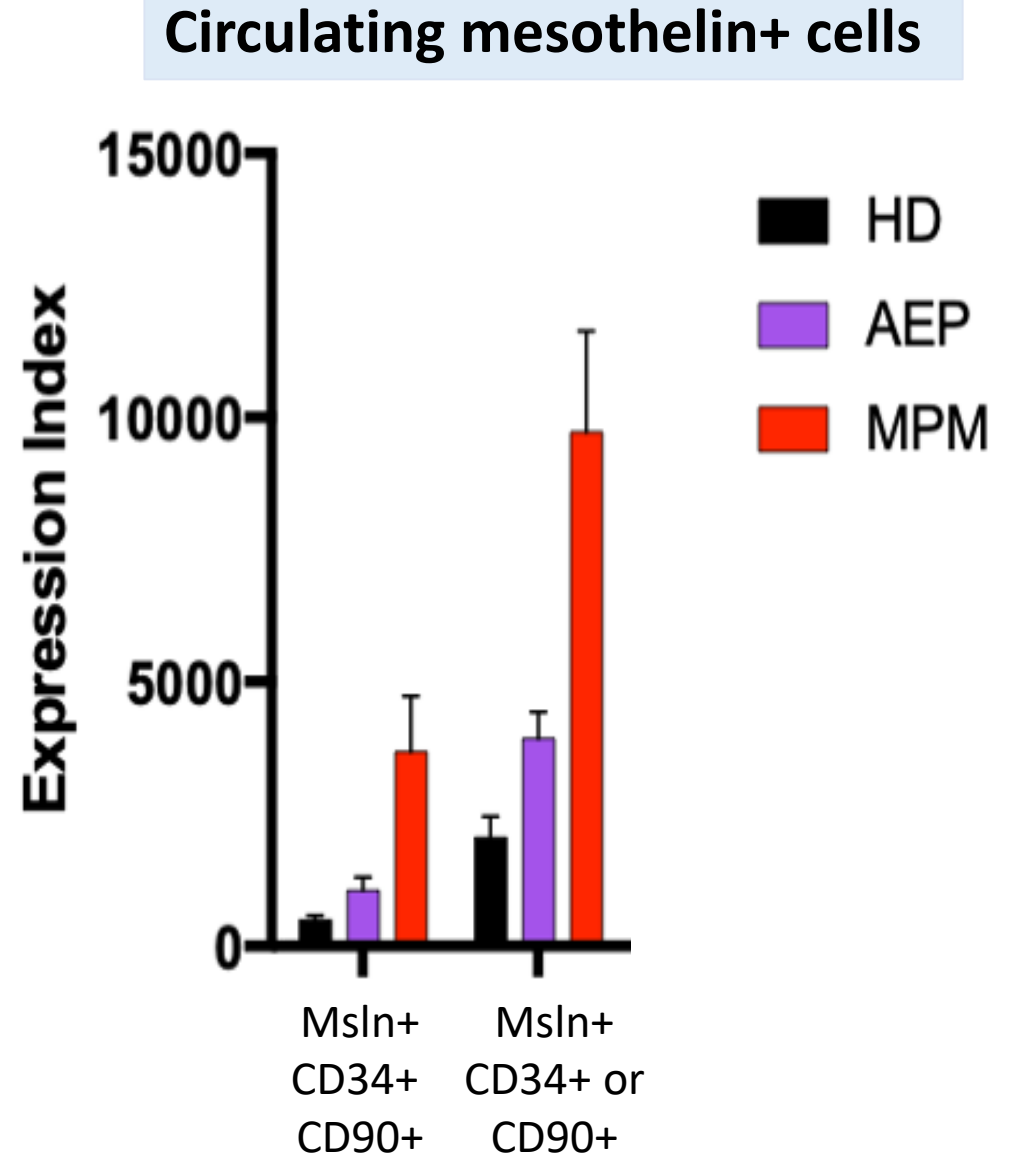


Blood



Presence of mesothelial progenitor cells after asbestos exposure and mesothelioma

1. HD: healthy donors (n=7)
2. Asb: asbestos-exposed individuals (n=31)
3. MPM: mesothelioma patients (n=38)



Conclusions

- Important role for screening in asbestos exposed individuals
- CT scan is not ideal for screening
- Blood based or breath condensate screening methods are more adequate
- Serum tumor markers are not (yet) used clinically for screening
- Circulating mesothelial progenitor cells may offer new opportunities for screening population at risk after asbestos exposure (study in preparation)



Thank you