

# Griffith University - Case for Support

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## Mesothelioma Research Program

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**Director, Griffith Health Institute**

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# Griffith Health Institute (GHI)

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- Established in 2007.
- Integrated health and medical research.
- Focus on chronic disease prevention and health innovation.
- Located within the Gold Coast campus of Griffith University:
  - will be directly linked to the Gold Coast University Hospital.
- Medical, Social, Health, Clinical and Biological Sciences.
- Preventative health and innovative healthcare outcomes.

# Areas of Expertise - Global, National, and Local Health Priorities

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- **Health Innovation:**
  - Including diagnostics, therapeutics and healthcare practices, to enable better clinical and community health outcomes.
- **Preventative Health:**
  - Lifestyle interventions to foster healthy communities and reduce the incidence of common chronic disease.
- **Health Determinants:**
  - Identification of clinical, social and psychological determinants of health to improve healthcare delivery, health promotion and health sustainability.
- **Epidemiology-Population Health:**
  - Identification of molecular and environmental factors in chronic disease susceptibility, development, prevention and treatment.

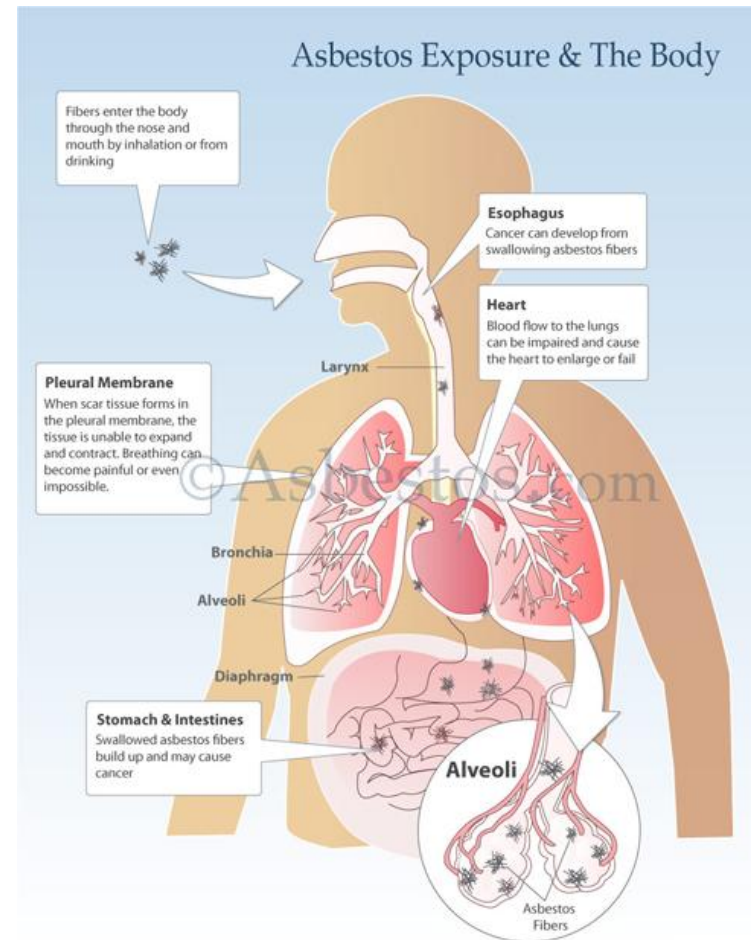
# Genomics Research Centre (GRC)

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- **Established in 1997.**
- **Part of the GHI, located on the GUGC campus.**
- **Unique population resources and their application to genetic studies of common, complex human disorders:**
  - Population, Functional, Clinical and Pharmacogenomics.
- **54 research staff:**
  - Including academic, postdoctoral, postgraduate, research assistants, research nurses.
- **600 sqm dedicated research laboratory:**
  - housing significant molecular infrastructure, cell and tissue culture, and cytogenetics.
- **NATA accredited DNA diagnostic testing and clinical trial capacity.**

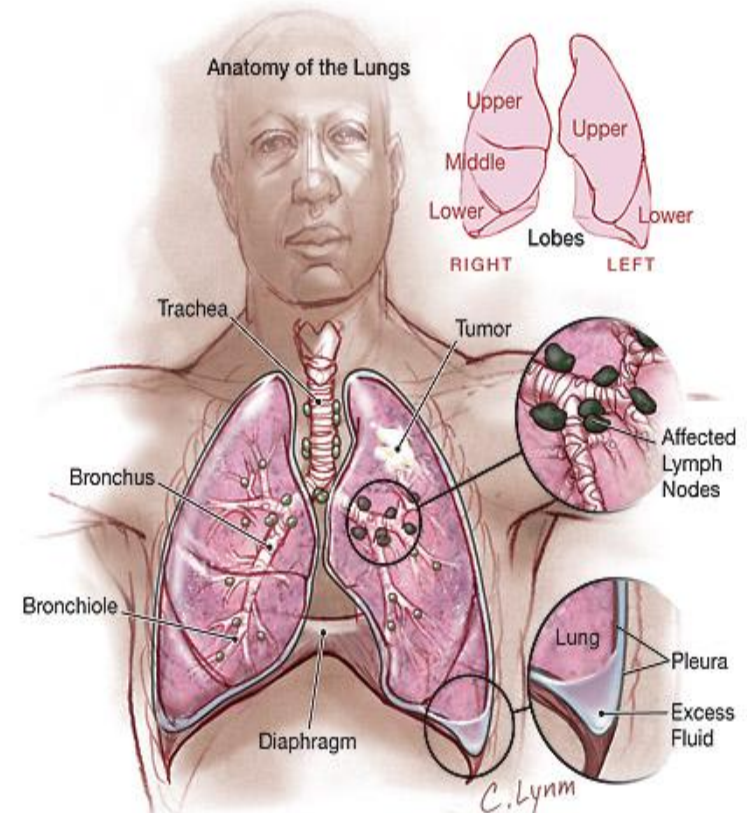
# Malignant mesothelioma

- Cancer originating from the lining (mesothelium) of the pleural and peritoneal cavities
- Before 1950, so rare, some pathologists questioned its existence
- Increasing use of asbestos after WWII led to better diagnosis
- Long latency (15-60 years) between exposure and onset



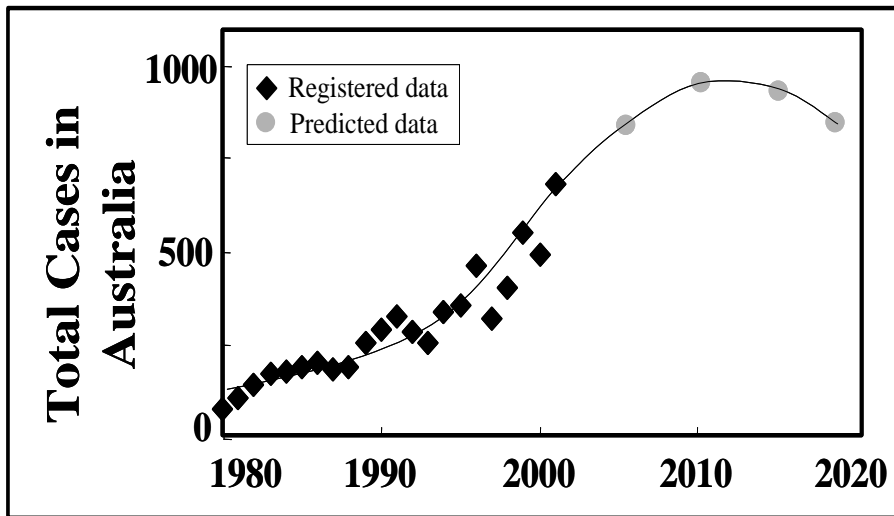
# Malignant mesothelioma

- Predominantly caused by asbestos
  - other mineral fibres (erionite, tremolite) also cause MM
- Resistant to a variety of established anti-cancer drugs
- Surgery ('de-bulking') only alleviates the pathology
  - sometimes combined with chemo-/radiation therapy
- Need to find more efficient and selective cures



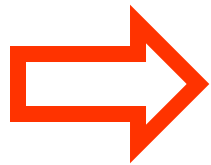
# Incidence of MM in Australia

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Leigh J and Driscoll T (2003) Malignant mesothelioma in Australia, 1945-2002. *Int J Occup Environ Health* 9, 206.

- **Currently:** some 800-1000 new cases per year
- The number of new cases will not decrease before 2015-2020
- More than 10 thousand lives at stake



**Hope for mesothelioma cure:  
MITOCANS**

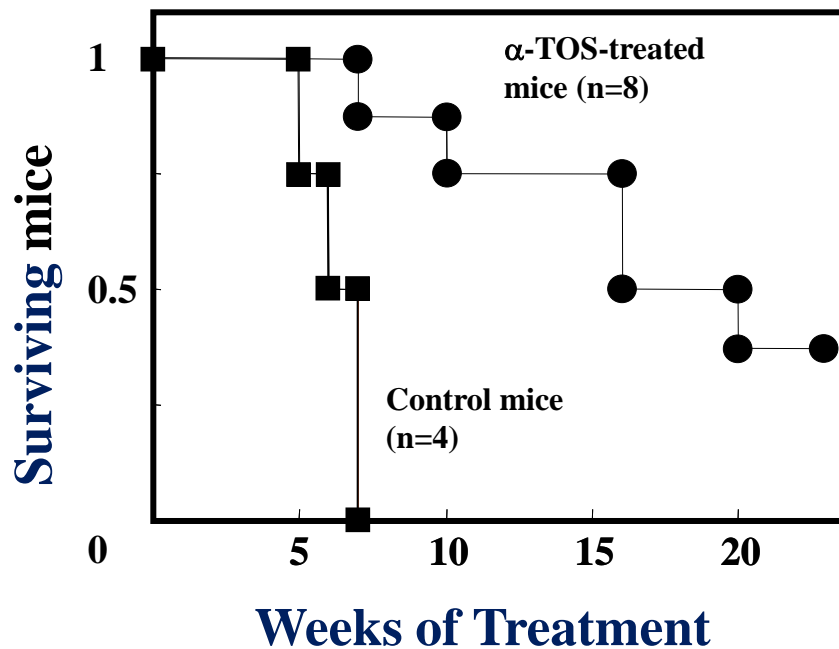
# MITOCANS

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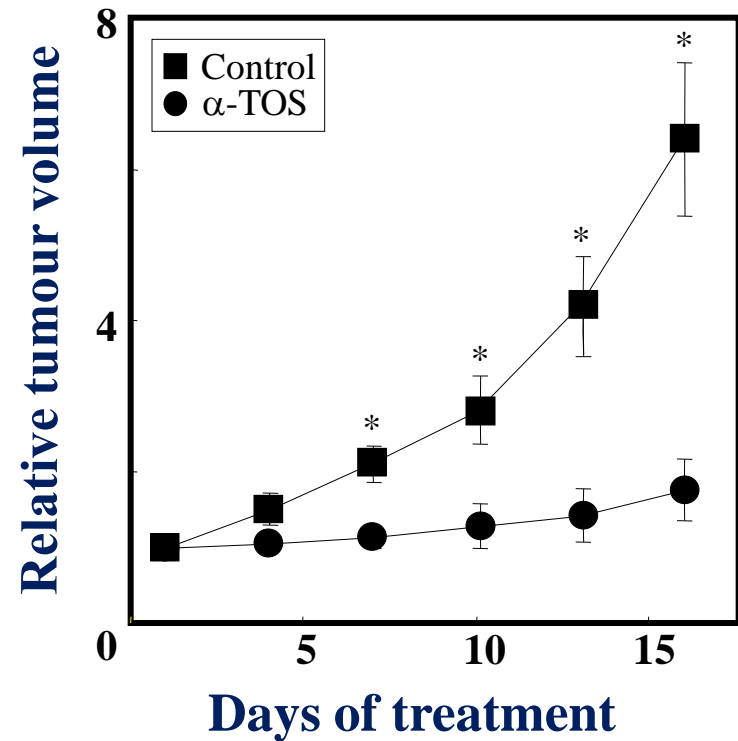
- **Mitocans (= mitochondria & cancer):**
  - small compounds selectively killing cancer cells
- **Mitocans target mitochondria - the power-house of the cell:**
  - suppress transfer of electrons (CII to CIII) causing apoptosis
  - genes for CII rarely mutate in cancers (1 in 1 million patients)
  - no mutations in CII known for mesothelioma
- **Vitamin E analogues: a class of mitocans:**
  - vitamin E succinate ( $\alpha$ -tocopheryl succinate,  $\alpha$ -TOS)
- **$\alpha$ -TOS is selective for cancer cells:**
  - induces apoptosis (activates cells own death pathway)
  - non-toxic to normal cells
- **$\alpha$ -TOS demonstrated a strong anti-cancer activity in animal models**

# Vitamin E succinate - mouse model

Human MM cells injected into peritoneum of nude mice



Human MM cells injected into nude mice subcutaneously



# Vitamin E succinate – case report

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- **One mesothelioma patient in Australia**
  - **Given  $\alpha$ -TOS transdermally**
  - **Survival increased by 3-4 years**
  
- **One mesothelioma patient in Europe**
  - **$\alpha$ -TOS applied transdermally**
  - **Patient currently doing fine, has been on  $\alpha$ -TOS therapy for less than one year**

# Transdermal therapy – How it works

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- Drug is applied to the skin, usually as part of an adhesive patch, for absorption into the bloodstream.
- Advantage of  $\alpha$ -TOS therapy
- No need for intravenous administration
- Sustained, slow delivery across the skin
- Can be self-administered by the patient



# Our expertise

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- **Research staff expertise:**

- Professor Lyn Griffiths – human molecular genetics of complex disease.
- Prof Jiri Neuzil – apoptosis, cell signalling, cancer prevention (Vitamin E).
- A/Prof Ming Wei – liver cancer, gene therapy and clinical therapeutics.
- A/Prof Steve Ralph – cancer therapy/prevention, vaccines, gene regulation.
- Dr Larisa Haupt – mesenchymal stem cells, breast cancer stem cells, ECM.
- Dr Albert Mellick – angiogenesis, bone marrow Stem cells, gene therapy.
- Dr Louise Alldrige – proteomics, ECM cell signalling, breast cancer.
- Dr Tracey Jason – clinical pharmacology, cancer target identification.
- Dr Robert Smith – gene expression, breast cancer.
- Dr Lanfeng Dong – apoptosis and targeted anti-cancer drugs

- **Cancer clinicians:**

- Dr Stephen Weinstein – Director of Pathology, Gold Coast Hospital.
- Dr Alfred Lam – Clinical Pathologist, Gold Coast Hospital.
- Dr Maher Gandhi – QIMR, lymphoma, viral therapeutics.

# Expected Research Outcomes

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- Expansion of models (mouse models):
  - Increase data set.
- Correlate with clinical data:
  - Increase recruitment and participation of clinical participants;
  - Improve uptake of drug (patches).
- Refine and further develop therapeutics:
  - Personalised gene-directed therapeutics;
  - Pharmacological intervention.

# Case for Support (Three-year period)

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- Novel research of medical, clinical and public health significance.
- Requires dedicated student/staff allocation:
  - Post-graduate research training.
- Minimum start-up costs:
  - approx \$25,000 per annum scholarship (\$75,000)
  - and approx \$25,000 over the three-year period for reagents and consumables, IT and administrative support  
~(\$100,000 in total).
- Research Program ongoing, graduate training over a three-year period.