# SUMMER RESEARCH 2024/25
# PROJECT ABSTRACT

THE UNIVERSITY OF WAIKATO
Te Whare Wānanga o Waikato

**PROJECT # 49**

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| **SUPERVISOR/S:** | Dr Linda Peters & Dr Archana Pandita Genetics |
| **PROJECT TITLE:** | of Breast Cancer in the Waikato Region |
| **FIELD:** | Molecular and Cellular Biology |
| **DIVISION/SCHOOL:** | HECS - Te Aka Mātuatua School of Science |
| **PROJECT LOCATION:** | Hamilton |
| **EXTERNAL PARTNER:** | Pathlab |


**PROJECT ABSTRACT:**

New Zealand has one of the highest rates of breast cancer. To date, a total of 17,477 new breast cancer registrations including 2536 Māori cases were reported in NZ during 2017-2021. This number includes 1518 breast cancer registrations in the Waikato Region (NZ Cancer Registry, 2024). There are also major ethnic disparities in breast cancer survival, with the statistics for Māori and Pacific women being much worse than other ethnic groups.

Patients diagnosed with breast cancer are routinely assessed for estrogen receptor (ER), human epidermal growth factor receptor-type 2 (HER2), and progesterone receptor status using immunohistochemistry. The ER receptor and HER2 status plays a pivotal role for deciding on treatment options. Breast cancers recur any time from a few months to several years after the primary diagnosis and treatment. Plus, there are multiple factors that can cause recurrence of the tumour, including incomplete resection, family history, drug resistance, germ line or acquired genetic alterations.

Mutations in ESR1 gene are known to occur in primary breast cancers (2.6-12%) but they are acquired more in metastatic hormone positive breast cancers (11-55%), mostly in endocrine-treated breast cancers. ESR1 mutations are thought to be associated with resistance to endocrine therapy (blocks the hormone estrogen, which keeps the cancer from growing).

Currently, there is insufficient information about the NZ incidence and clinical implication of these mutations in early recurrence events, local or metastatic. Thus, this pilot study will determine the incidence of the four most common ESR1 mutations in hormone-positive stored breast tumour samples from a Waikato patient cohort and how well the corresponding treatment therapy was for these individuals.

The aim of this research is to (1) detect the rate of four ESR1 mutations in primary and metastatic breast carcinomas treated with endocrine therapy in the Waikato region using amplified DNA extracted from archival tumour samples (approx. 100 cases, from 2017 onwards due to advances in treatment options) with high resolution melting; (2) statistically analyse the recurrence-free interval and overall breast cancer survival using Kaplan-Meier survival plots; and (3) assess if the mutations have significant prognostic index for management purposes. No ethic data will be included or evaluated.


**STUDENT SKILLS:**

- Completed SCIEN100 (Science and Mātauranga Māori) and BIOMO202 (Introduction to Genetics)
- Confident using statistical programmes
- Excellent interpersonal and communication skills

**PROJECT TASKS:**

1. Receive training to work in a Physical Containment 1 Laboratory and the D2.20 Histology Room at the University of Waikato.
2. Archival tumour samples from breast cancer patients treated with endocrine therapy prior to and after local/metastatic recurrence will be collected for analysing four hot spot mutations of ESR1 using a high resolution melt curve assay (approx. 20 cases). This is a small pilot study into the genetics of breast cancer in the Waikato region. It does not include any ethnicity data.

3. DNA will be extracted from formalin-fixed paraffin embedded tissue blocks (deidentified), amplified using a high resolution melt assay at the University of Waikato using their equipment for mutational analysis.
4. Amplified DNA will also be confirmed by Sanger Sequencing and aligned with the ESR1 reference nucleotide sequence.
5. Collect and analyse data by using a statistical program such as SigmaPlot (Systat Software, Inc, San Jose, CA).
6. Attending meetings to consult and partner with Māori and Pacifica to work towards including informed consent and collecting ethnicity data on the next project as part of a larger grant such as Health Research Council.
7. Communicate their final research findings in the form of a:
    - PowerPoint presentation to the laboratory during a University of Waikato C2 Molecular group meeting;
    - Poster at the End-of-Summer Scholarship Programme.

**EXPECTED OUTCOMES:**

- Student's Research Poster (as per clause 6 of the Scholarship regulations)
- Determine the ESR1 mutation status of 20 breast cancer patients using high resolution melt curve analysis and Sanger Sequencing. The results of this pilot study will inform the next stage of the project. Our aim is to increase the sample size and include ethnicity data but with significant input and partnership with Māori and Pacific Peoples regarding experimental design, informed consent, and ownership/dissemination of the data.