New Method of Measuring Mammary Epithelial Cell (MEC) Turnover \textit{in vivo}

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Abstract

Clinical studies have shown that rates of cell turnover is a central characteristic of tumors, and that elevated rates are associated with tumor growth and the risk of developing cancer. In contrast, the rate of cell turnover in normal human breast is about one cell division per month. We have recently worked out how to apply a technique that has proven to successfully label and measure cell division rates directly, accurately and safely in people, without use of radioactivity or toxic metabolites (Proceedings of the National Academy of Sciences, USA, 1998).

In this paper, we describe how to apply this technique to study both cancerous and normal cells within and outside of the breast. The objectives of the present study are three-fold: first, to demonstrate that the technique is valid and can be applied in humans as well as animals; second, to determine what genistein, a potent cancer preventative agent in rats (found in soybeans) does to breast cell proliferation; and, third, to establish normal rates of breast cell division in humans and the factors that are associated with variability between women (age, weight, ethnic origin).

The aims of our study are three-fold:

1. To verify that a safe, effective method of measuring mammary epithelial cell proliferation in vivo can be used in humans.
2. To develop a method of measuring the effect of Genistein (a soy component) on MEC proliferation in normal and pre-cancerous stages of breast development.
3. To establish normal rates of breast cell division in humans of different age, ethnicity, and risk groups.

Methodology

Our laboratory has developed a method to label the DNA of dividing cells with a stable (non-radioactive) isotope of water and thereby determine the percentage of new cells by GC/MS* analysis. This method was originally developed to measure cell division rates of normal and cancerous breast epithelial cells (the cells that become breast cancer) in animals and humans. The objectives of the present study are three-fold: first, to demonstrate that the technique is valid and can be applied in humans as well as animals; second, to determine what genistein, a potent cancer preventative agent in rats (found in soybeans) does to breast cell proliferation; and, third, to establish normal rates of breast cell division in humans and the factors that are associated with variability between women (age, weight, ethnic origin).

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Analytical Methods - All Studies

1. **In vivo** estradiol
2. Urine is collected ½ way through the labeling period (7-14 days)
3. **Core biopsies of each quadrant, and a core biopsy of tumor aspirations can be used instead of core biopsies to acquire breast tissue
4. **2H2O injections and drinking water same as Study #1**
5. **Subject Age Menstrual Status 2H20 Dose Days Labelling Plasma 2H2O% New Cells**
6. **Study #3 Results**

Study #1 Results

- **Subject Age Menstrual Status 2H20 Dose Days Labelling Plasma 2H2O% New Cells**
- **Study #2 Methods**
- **Study #2 Results**
- **Study #3 Methods**
- **Study #3 Results**

Conclusions

- **Subject Age Menstrual Status 2H20 Dose Days Labelling Plasma 2H2O% New Cells**
- **Study #1 Results**
- **Study #2 Methods**
- **Study #2 Results**
- **Study #3 Methods**
- **Study #3 Results**

Utility of Method

- **Genito vasculäre Biomechanik von Brustbereich.**
- **Diagnostic tool for early detection of breast cancer**
- **Use for monitoring effectiveness of current prevention interventions**
- **Use for measurement of cancer treatment effectiveness**