

Cancer Etiology Studies with the Help of Patient Sera

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The value of serum banks for epidemiologic research has long been recognized¹. Banks of specimens from diseased persons are useful for characterizing disease².

Alert clinicians have played a key role in recognizing environmental and genetic influences in cancer etiology^{3,4}. Julia Landin e.g. has described balanced translocations in 2 of 7 patients with pancreatic neuroendocrine tumors⁵.

Sera have been obtained from 753 consenting patients in a medical oncology practice in the years 1983 to 1991 and stored at minus 70 degrees Celsius. They allow etiology studies of the following types :

Single Person Study

It could be tested if a deceased patient belongs to a suspected Li Fraumeni family by searching for a TP53 mutation in serum DNA.

Family Study

There are sera from persons belonging to 5 colorectal cancer families with identified germline mutations. Mutation carriers could be identified by examining serum DNA.

Cohort Study

Chronic lymphocytic leukemia (CLL) has a strong hereditary component, but an understanding of predisposition genes is poor. In the practice cohort of 66 patients with CLL Patrick Maurer has found that 23 patients (34%) had multiple malignancies and that 46 (12%) of first degree relatives had malignancies with overrepresentation of CLL and upper GI

¹ Evans AS : Serological surveys : The role of the WHO serum reference bank. WHO chronicles 21 : 185-190, 1967.

² Winn DM, Reichman ME and Gunter E : Epidemiologic issues in the design and use of biologic specimen banks. Epidemiologic Reviews 12 : 56-70, 1990.

³ Miller RW: Rare events as clues to cancer etiology: the eighteenth annual Symposium of the Princess Takamatsu Cancer Research Fund. Cancer Research 48 : 3544-3548, 1988.

⁴ Weber W : Krebsforschung in der Praxis. Schweiz. Rundschau Med (PRAXIS) 81: 1069-1073, 1992.

⁵ Landin J and Weber W: Etiological observations in seven patients with pancreatic neuroendocrine tumors (PNETs). In vivo 30: 147-148, 2016.

malignancies⁶. Sera of 38 of the 66 CLL patients are in the serum bank, in which susceptibility genes could be looked for.

Agnostic, genome-wide searches for genetic susceptibility could be done in cohorts of the serum bank, such as 31 patients with ovarian carcinoma, 17 Hodgkin, 11 prostate or 9 pancreatic carcinomas etc.

We have shown that current next generation sequencing technology is sufficiently robust and specific to analyze our sera⁷.

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⁶ Weber W, Maurer P, Estoppey J and Zwahlen M: Chronic lymphocytic leukaemia: clinical-aetiological findings in 66 patients and their families. *Hereditary Cancer in Clinical Practice* 5: 210-212, 2007.

⁷ Ritter M, Paradiso V, Widmer P, Garofoli A, Quagliata L, Eppenberger-Castori S, Soysal SD, Muenst S, Ng CKY, Piscuoglio S, Weber W and Weber WP: Identification of somatic mutations in thirty-year-old serum cell-free DNA from patients with breast cancer: a feasibility study. *Clinical Breast Cancer* 20: 413-421, 2020.