a. Microarray Used in Ovarian Cancer—The Spentzos Study

In a study of ovarian cancer, Spentzos et al. (90) acquired tumor biopsies from 68 patients and analyzed the expression of a large number of genes. Treatment involved surgery followed by chemotherapy. In general, ovarian cancer is eradicated in 70% of cases, but the cancer usually returns, and when it returns it is unusually resistant to chemotherapy.

What is thus desired is a prognostic device to determine which patients will likely fail initial therapy. In the Spentzos study, ovarian tumor biopsies were collected at the time of surgery, but before chemotherapy. For their first study, seven samples from short-term survivors and seven samples from long-term survivors were analyzed. The result was a first list of genes, where changes in expression were associated with short-term survival, and a second list of genes where changes were associated with long-term survival. Then, after the surgery, patients received chemotherapy, and study personnel waited several years to determine which patients would be short-term survivors (death within 2 years), and which would be long-term survivors (over 5 years).

After collecting all survival data, the researchers sought a correlation between survival and gene expression, and arrived at a collection of 115 genes, which they named, "Ovarian Cancer Prognostic Profile."

With this profile in hand, the researchers applied it to a group of 68 patients, who were also treated with surgery, followed by tumor biopsy and gene analysis, and then chemotherapy. The authors drew a Kaplan–Meier plot. The first curve on the plot contained data points corresponding to all patients with a gene expression profile that, according to their diagnostic device, had a favorable prognosis. The second curve on the plot contained data points corresponding to all patients with a gene expression profile that, according to their diagnostic device, had a poor prognosis. The result was two well-separated curves on the Kaplan–Meier plot, where the degree of separation was measured by the hazard ratio (HR). The separation was statistically significant ($P = 0.004$). The authors concluded that patients showing an unfavorable prognosis would be appropriate candidates for maintenance therapy, or for treatment with new experimental drugs.

b. Microarray Used in Colon Cancer—The Wang Study

In a study of Dukes' B colon cancer, Wang et al. (91) acquired tumor biopsies from 74 patients, prepared cDNA from the biopsies, and analyzed the cDNA using a microarray that contained DNA corresponding to 22,000 different genes. (The term Dukes' is not a typo.) In the years following surgery, 31 patients had relapse within 3 years, whereas 43 patients remained cancer-free for over 3 years.

Eventually, the authors arrived at a 23-gene signature that served as a prognostic device.

With this device in hand, the authors studied a separate group of patients (36 patients). During surgery for the colon cancer, the researchers acquired tumor biopsies, analyzed each tumor sample with the 23-gene signature device, and allocated each patient into the good prognosis group or the poor prognosis group. Then, the researchers waited 6 years, and kept records of the survival time for each

[90]Spentzos D, Levine DA, Ramoni MF, et al. Gene expression signature with independent prognostic significance in epithelial ovarian cancer. J. Clin. Oncol. 2004;22:4700–10.

[91]Wang Y, Jatkoe T, Zhang Y, et al. Gene expression profiles and molecular markers to predict recurrence of Dukes' B colon cancer. J. Clin. Oncol. 2004;22:1564–71.