The following introduces C-reactive protein (CRP) into this narrative. In view of the fact that serum amyloid A is an "acute phase protein," the authors also sought correlations between other established acute phase proteins, such as CRP, and survival to melanoma. The Findeisen study discovered that CRP expression was able to distinguish between poor prognosis Stage I melanoma patients and good prognosis Stage I melanoma patients. The authors concluded that the combination of expression data on serum amyloid A and CRP serves as an excellent prognostic biomarker for early stage melanoma patients. Findeisen et al. (109) were also careful to note that serum lactic dehydrogenase (LDH), a traditional biomarker for advanced melanoma, failed to have any prognostic significance for early stage melanoma.

c. Methodology tip – identifying new biomarkers by mass spectroscopy

The technique of mass spectroscopy used by Findeisen et al. (110) involved immobilizing proteins on a surface, washing away unbound proteins and lipids, ionizing the bound sample with a laser, and detecting the mass/charge ratio of vaporized peptides. In this technique, an organic solution containing "energy absorbing molecules" is applied to the immobilized proteins prior to ionization. These molecules can include sinapinic acid, 2,5-dihydroxybenzoic acid, or alpha-cyano-4-hydroxycinnamic acid (111,112,113,114). The protein dissolves into the organic solvent and the solution dries, forming crystals containing the protein and the energy absorbing molecules. Then, a laser illuminates the sample, causing ionization and desorption, and the ionized peptides enter the gas phase. The ionized peptides then move quickly away from the surface with the application of a voltage. Peptides with a positive charge "fly away" from the surface and the mass spectrometer measures mass-dependent flight times. From this measurement, the instrument calculates the mass/charge (m/z) ratio.

d. C-reactive protein and atherosclerosis

In addition to expression by hepatocytes, CRP is also expressed by cells in atherosclerotic lesions, an event expected to result in local concentrations of CRP that are far

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[110] Findeisen P, Zapatka M, Peccerella T, et al. Serum amyloid A as a prognostic marker in melanoma identified by proteomic profiling. *J Clin Oncol*. 2009;27:2199–2208.

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