

Protein Modifications in Human Breast Cancer

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Breast cancer was the second leading cause of cancer related mortality for females in 2014. By exploiting the ultrahigh mass resolution of high-magnetic-field ion cyclotron resonance, we here isolate an individual “proteoform” (i.e., a protein with a particular combination of mutations and chemical modifications) as gas-phase ions. We then dissociate the ions to weigh the fragments, then identify and quantitate the mutated or modified site(s) as breast cancer cells progress through their cell cycle.

We find histone proteins H1.2 and H1.4 metastatic breast cells of type MDA-MB-231, whereas an additional histone variant, histone H1.3, is seen only in non-cancerous MCF-10A cells. Notably, phosphorylation of histones H1.2 and H1.4 increases significantly during cell division (mitosis, or the “M phase”), suggesting that these events are cell cycle-dependent and may serve as biomarkers for proliferation of cancer cells during breast cancer invasion. T146 and T154 are the only phosphorylated sites observed at higher rates in metastatic versus non-neoplastic cells.

These experiments require the ultrahigh mass resolution provided by NHMFL’s 14.5 T Fourier Transform – Ion Cyclotron Resonance (FT-ICR) mass spectrometer due to the complexity of the resonance peak patterns from the fragment ions.

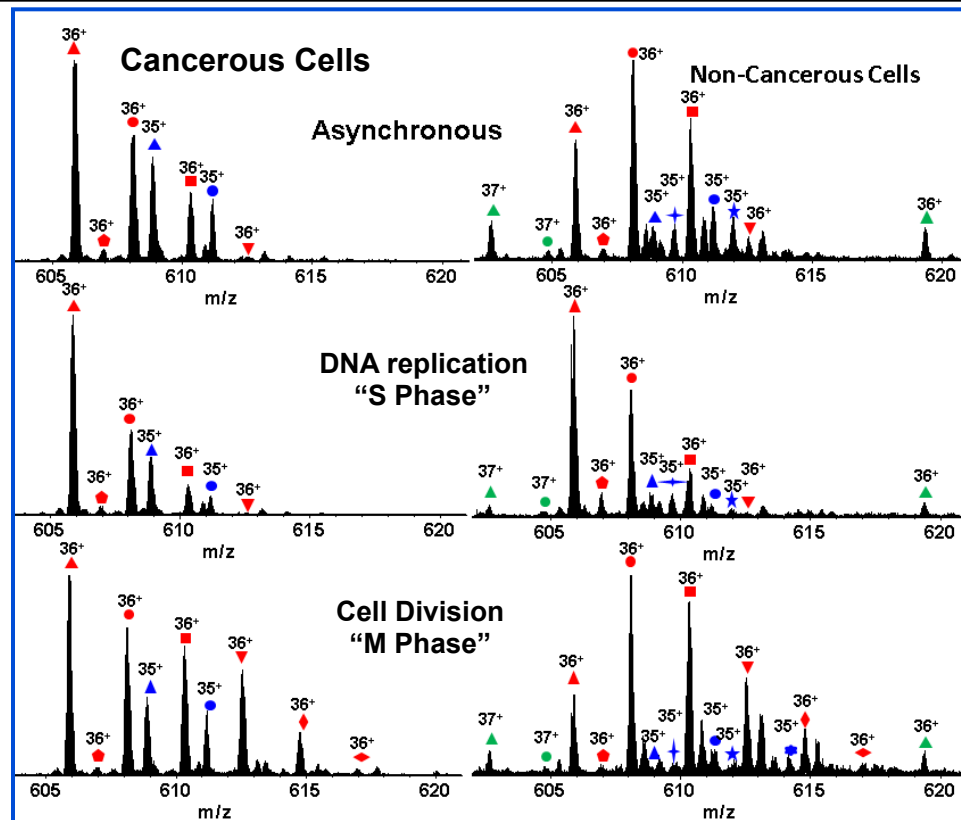


Figure 1: FT-ICR mass spectra annotated for the proteoforms observed in (left) cancerous and (right) non-cancerous cells. Cells were grown asynchronously (at top) or blocked during DNA replication - the “S phase” - (at middle) or during mitosis - “the M phase” - (at bottom). Proteoforms (different symbols) for H1.2, H1.3 and H1.4 are shown in blue, green and red.

Facilities: 14.5T Ion Cyclotron Resonance Magnet, NHMFL/FSU
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