Proteomic analyses in Waldenstrom's Macroglobulinemia (WM).

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gonucleotide microarray technologies have become powerful tools for the molecular classification of nan neoplasias. However, gene expression profiling, while indicative of potential functional interactions, not serve to fully characterize them, in part because of multi-factorial regulation of protein expression function at post-transcriptional and post-translational levels. A prime example of this concept is the ing of cell signaling pathways: their key role in mediating interactions of tumor cells with their milieu modulating their growth/survival is dictated by post-transcriptional modifications (e.g. sphorylation) of its components, which cannot be directly monitored with transcriptional profiling. To ain further insight into the biology and pathophysiology of WM, we have therefore performed proteomic lysis of the signaling state of WM cells using multiplex immunoblotting arrays, which has allowed the racterization of levels and/or phosphorylation state of >100 kinases and kinase targets implicated in naling cascades with key roles in cell growth, survival, migration, transcriptional/translational control . In particular, we performed comparative proteomic studies of the signaling state of WM vs. multiple eloma (MM) cells at baseline, as well as in the setting of treatment of these tumor cells with ventional (e.g. dexamethasone) or novel anti-tumor agents. Through these studies, we found that the teomic profiles WM and MM cells share significant overlap, which presumably reflects the presence, in h diseases, of key components of a proteomic signature of the B-cell lineage. On the other hand, there also important qualitative and/or quantitative differences in respect to several individual signaling teins. These findings may reflect putative molecular differences of WM vs MM, related to their distinct ogeny. This dual picture is also evident in comparative studies of drug-treated proteomic profiles, which eal both proteomic targets with comparable patterns of drug-induced modulation across both these 2 sma cell dyscrasias, as well as other proteins which are differentially affected by drug treatment. These ferential molecular events may provide insight into the variable degrees of sensitivity of WM vs MM s to certain anti-tumor agents. Importantly, these findings reinforce the notion that, at the molecular el, WM and MM share significant common denominators, but also have key differences. While the ner ones may explain the overlap in the therapeutic options available for these diseases, the latter ones icate that novel therapies rationally designed to capitalize on the distinct molecular features of WM may required to improve the outcome of patients with this presently incurable disease.