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OVERVIEW

Regulatory Surrogate Endpoint Biomarkers

The role of several known growth factors, growth factor receptors, and hormone receptors in breast cancer progression were reviewed in the "Regulatory Surrogate Endpoint Biomarker" session. Carlos Arteaga (Vanderbilt University School of Medicine, *Nashville*, TN) presented the first talk, focusing on the role of TGF-βs in breast cancer progression. He presented data showing that transfection and overexpression of TGF-β1 in human breast cancer cells confers estrogen-independent growth to breast cancer cells in a nude mouse model system. Thus, overexpression of this growth factor bypasses normal estrogen growth control pathways, leading to autonomous growth. Conversely, Dr. Arteaga presented intriguing data suggesting that abrogation of TGF-β1 and -β2 expression by anti-TGF-β antibodies inhibits tumor formation and metastatic growth of MDA-MB-231 breast cancer cells in nude mice. These data suggest that TGF-β may play a role in both the development of estrogen-independent growth and tumor progression. The clinical implications of these observations are clearly evident, and suggest that a careful examination of TGF-β expression in breast cancer and its role in early breast disease should be rapidly explored.

The second talk was presented by Dennis Slamon from the University of California, Los Angeles. He focused on the role of the HER-2/*neu* oncogene in breast carcinogenesis, presenting preclinical data that inhibition of HER-2/*neu* expression by monoclonal antibodies directed against the extracellular domain of the receptor can suppress xenographic growth both *in vitro* and *in vivo*. Clinical trials are currently underway testing this new strategy to inhibit breast tumor progression. In addition, Dr. Slamon's laboratory is actively involved in determining the role of the various HER-2/*neu* ligands in the HER-2/*neu* growth factor receptor cellular signaling pathway.

The last talk of the session, presented by Suzanne Fuqua (University of Texas Health Science Center, San Antonio, TX), dealt with the role of the estrogen receptor (ER) and specific variants of the receptor in antiestrogen resistance and progression. She presented data showing that one ER variant, truncated for the ligand binding domain, is associated with tamoxifen resistance in breast cancer. Furthermore, she presented a model hypothesizing that ER alterations may be one of the first genetic changes in early breast disease which may be involved in driving breast proliferation and eventual breast cancer progression.

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