RESIDENTS' TAKE: Advances in Science and Medicine Catalyzed by Pioneering Skin Research, Montagna Symposium 2011 60th Anniversary

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Eleven Dermatology residents from Oregon Health & Science University attended the 60th anniversary Montagna Symposium on the Biology of Skin and learned of recent scientific discoveries in dermatologic research melding past seminal triumphs with new applications for the prevention and treatment of skin diseases. Engaging the research presentations from the meeting, this summary focuses on the residents' take on potential future applications in clinical dermatology.

Investigators highlighted potential pathways for future intervention in the prevention of skin cancer and aging. Laura Niedernhofer described examples of DNA repair mutations in ERCC1 leading to both carcinogenesis (hyperproliferative state) and aging (loss of regeneration) and downstream mediators of these mutations. Amanda McCullough showed topical application of bacterial DNA repair enzymes reverses cyclobutane-pyrimidine-dimer formation. Topical delivery of DNA-repair enzymes with TAT-mediated translocation into the epidermis may lead to therapeutic drug development for the primary prevention of skin cancer as well as skin aging.

Major advances in treatments of advanced basal cell carcinoma (BCC) were described during the meeting session on Hedgehog signaling. Silvia Buonamici showed that NVP-LDE255, a Smoothened inhibitor, prevents progression and reduces the burden of existing BCCs. Similarly, Ervin Epstein demonstrated that Vismodegib can result in complete remission of existing BCCs while preventing the development of new tumors in patients with Gorlin Syndrome. In both studies, significant adverse effects, including myalgias, alopecia, and dysgeusia, were reversible after discontinuation of the drug, but perhaps more importantly from a clinical perspective, tumors that had regressed recurred after cessation of therapy.

Angela Christiano discussed the discovery of numerous novel genes associated with alopecia areata (AA), including CTLA4 and NKG2D. Inhibiting CTLA4 co-stimulation with abetacept, which is used in the treatment of rheumatoid arthritis, or an IL-15 inhibitor targeting NKG2D could be effective in the treatment of AA.

Jakub Tolar demonstrated that stem cell transplantation corrects skin protein deficiency in children with epidermolysis bullosa, though the corrective mechanism remains unknown. With the aid of new markers and molecular techniques, epithelial stem cells are giving up their secrets, including the critical role the microenvironment plays in determining stem cell fate. But can tissue stem cells be "reprogrammed" by a new microenvironment or do they retain a resolute "memory" of their origin? As long as these questions remain unanswered, the full therapeutic promise of stem cells goes unrealized.

Important investigations in cancer biology have addressed how malignant cells gain metastatic capabilities and how those cells differ from malignant cells that remain in the original tumor. Ian Mackenzie discussed distinct stem cell populations in cutaneous squamous cell carcinoma (SCC) with different metastatic potential and different responses to treatment modalities. His findings have important implications in how we understand and treat cutaneous and metastatic SCC.

Addressing complex tissue allograft transplantation challenges, investigators aimed not only to minimize rejection response but also to reduce requirements for long-term immunosuppression. Kathryn Wood focused on harnessing the regulatory capacity of host Foxp3+ Tregs to minimize the rejection response to human allografts. Shay Soker described decellularized "natural tissue" scaffolds populated with autologous differentiated stem cells to recreate a viable functional organ to be transplanted back into host. It is hoped that the host response to transplantation of these organs seen in early studies is an innate inflammatory rather than adaptive t-cell mediated response and therefore would not require long-term immunosuppression. These studies may have a significant impact not only on how successfully we perform and maintain tissue and organ transplants but also on the quality of life of transplant patients.

The 60th Montagna Symposium on the Biology of Skin highlighted past seminal research that has dramatically changed the landscape of our specialty. New applications in skin cancer prevention and aging, immunomodulation, and stem cells are on our doorstep for breakthroughs in clinical dermatology.