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Medscape Medical News

ASHG 2008: Many Squamous Cell Tumors in Organ Transplant Recipients Contain Nonrecipient DNA

Jacquelyn K. Beals, PhD

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November 19, 2008 (Philadelphia, Pennsylvania) — Genotypic analysis of DNA from cutaneous squamous cell carcinomas (SCCs) in organ-transplant recipients (OTRs) has identified extra alleles in some tumors. Normal tissues contain 1 or 2 alternative forms (alleles) of each gene. SCC tumors contain the alleles found in recipient tissues and, in some cases, 1 or 2 additional bands not of recipient origin. Studies are underway to determine whether donor cells are the source of these alleles and, more importantly, the source of the tumors.

Amanda Toland, PhD, presented work on nonrecipient DNA in SCCs of OTRs here at the American Society of Human Genetics 58th Annual Meeting. Dr. Toland is assistant professor in the Department of Molecular Virology, Immunology, and Medical Genetics, and Department of Internal Medicine's Division of Human Genetics, Ohio State University College of Medicine, in Columbus.

Dr. Toland told *Medscape Pathology & Lab Medicine* what caught their attention. "When we were looking at the genotype in the tumors, compared with normal [tumors], normally you have 2 alleles, 1 from mom and 1 from dad. And in the tumors, often ... we're seeing 3 alleles, and occasionally 4," said Dr. Toland. "That is not normal, and it didn't fit with any other things that we know normally happen during tumor biology. And it was very consistent in that particular tumor from multiple regions in the genome."

More than 1 million cases of nonmelanoma skin cancer occur in the United States each year, and 230,000 of these are SCC. Typically, SCC is associated with low mortality, resulting in 3000 deaths per year; only 2% to 5% of SCCs metastasize.

In OTRs, the risk for cutaneous SCC is 65 times higher than in nonrecipients. The risk of developing SCC in the 10 years after receiving a donor organ ranges from 10% to 45%. These tumors are also more aggressive, with 7% metastasizing. More than a quarter of all heart transplant recipients eventually die as a result of SCCs.

Subjects in the initial study were OTRs who had 5 or more SCCs. Investigators obtained normal and tumor DNA genotypes from each individual, and found extra alleles in 1 or more tumors in 11 of the 44 subjects. Extra alleles were never found in SCCs in non-OTRs.

Of the 5 female OTRs whose tumor DNA showed extra bands, 3 tested positive for the Y-chromosome-specific sex-determining region marker (SRY). All female controls were negative for SRY. Tumor DNA from the 6 male OTRs and the 2 females negative for SRY was genotyped for X-chromosome markers: 2 males and 1 female were found to have extra bands for X-specific markers, suggesting that their transplants were from female donors.

One challenge facing clinicians is balancing the immunosuppressive drugs and the increased risk for cancers in OTRs. "I think we've got a lot more work to do to figure this out," observed Dr. Toland. "For a lot of the patients who are getting multiple SCCs, [their physician is] already fiddling with their immunosuppressive dose to try to decrease the number of cancers they get.

"Obviously, heart transplant patients really need to keep very high levels [of immunosuppressive drugs], so it's harder to adjust those. I think if we can understand whether the donor cells are causing the cancer or are simply there ... there's a big difference between cells actually causing cancer and being in the environment of a cancer," Dr. Toland noted. "That's a huge connection we still need to make."

Medscape Pathology & Lab Medicine talked with session comoderator Cynthia C. Morton, PhD, professor of Obstetrics, Gynecology and Reproductive Biology and Pathology, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts, about screening donors for previous cancers or oncogenes.

"Presumably, there is clinical information that's available when the organ is harvested about the [donor], and maybe 1 question would be whether or not that patient ever had any type of skin cancer. But...you still wouldn't know whether 100% of them would be [screened]," said Dr. Morton. "You still need that organ, and you're going to die without the organ. Do you take the chance?

"There are many trade-offs like that in life now. If you have breast cancer and you need chemotherapy, there's a risk that later on you'll develop leukemia or a lymphoma. But what is your choice? Will you take that risk? I think that it will be really good to follow-up these data and to try to find out what type of information you can," Dr. Morton concluded. "But...what I hope is that we really will be successful with tissue engineering and will be making organs for people in the future that will be their own organs — and that will avoid these issues."

Dr. Toland and Dr. Morton have disclosed no relevant financial relationships.

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