ER IH

Fwd: Re: Lori A. Reigert Tissue Samples

Richard P. Stuart <rstuart@wowway.biz>
Tue 3/12/2019 9:04 PM
To: mrsrmrr@hotmail.com <mrsrmrr@hotmail.com>

-------- Original Message --------
Subject: Re: Lori A. Reigert Tissue Samples
Date: Tue, 12 Mar 2019 23:02:45 +0000
From: "Bastian, Boris" <Boris.Bastian@ucsf.edu>
To: "Richard P. Stuart" <rstuart@wowway.biz>

Dear Mr. Stuart,

We have sequenced the DNA of the tumor and normal cells to identify any genetic alterations commonly found in cancers, including melanomas, to assist with identifying the tissue of origin of Lori's cancer. Our methods surveyed approximately 500 cancer-related genes for mutations and approximately 40 for structural rearrangements such as translocations and assessed the entire genome for copy number changes.

Our analysis has yielded the following findings:

1) an absence of melanoma-typical mutations in driver genes such as BRAF, NRAS, GNAQ, GNA11, HRAS, NF1, SPRED1
2) a very low mutation burden, with an estimated number of somatic mutations of 1 per million bases. Melanomas on sun-exposed skin typically have a 20 to 200 fold higher mutation burden.
3) An absence of frequent high-level amplifications, which are common in melanomas on sun-shielded sites, including mucosal melanomas and acral melanomas
4) A deep deletion of the CDKN2A/B gene
5) the presence of an EWSR1-ATF1 in-frame fusion. This gene fusion results from a translocation between chromosomes 12 and 22 and is not known to occur in bona fide melanomas. Instead this fusion occurs in a variety of soft tissue tumors, such as Ewing's sarcoma, angiomatoid fibrous histiocytoma, and clear cell sarcoma (CCS).

Interpretation:
Based on the absence of melanoma-typical oncogenic alterations, the absence of a high mutation burden typically of cutaneous melanoma, and the absence of frequent amplifications typically of mucosal and acral melanomas the diagnosis of melanoma is highly unlikely. The presence of the ESWR1-ATF1 and the reported immunohistochemistry results render CCS the most likely diagnosis for this tumor. CCS is also called "melanoma of soft parts", because it typically expresses melanocytic markers by immunohistochemistry, whereas the others do not. Lori's tumor was positive for HMB45 and S100, consistent with this interpretation. Despite the expression of these markers CCS is now no longer considered a to be a tumor of melanocytic origin but a soft tissue tumor.

In summary, I think the genetic analyses provided an answer to Lori's parents' question about the nature of her disease. CCS is a still poorly understood disease, which is difficult to treat once it

metastatic, and I am sure any future research support in that direction would make a difference to future patients.

I hope that my analysis was helpful. Please don't hesitate to contact me, if you need additional information or would like to discuss the findings in person. Please send my regards to the Reigert Family and thank them for their support!

Best regards,
Boris Bastian

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On 1/28/19, 9:46 AM, "Richard P. Stuart" <rstuart@wowway.biz> wrote:

Dear Dr. Bastian,

I am contacting you at this time to confirm that you received the tissue samples regarding Lori Reigert. I also want to make sure
that the samples are sufficient for your testing purposes. Finally, my clients have contacted Lindsay Kopecky via email, but to date
has not responded. My client wants to know if their proposed donation of $3,000.00 is sufficient,who to make the check payable
and to what address to mail.

As always thank you for your time and consideration.

Best regards,

Richard Stuart, Esq.