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Detection of Tumor DNA in Plasma Using Whole Genome Amplification

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Abstract: Altered microsatellite DNA in the blood of cancer patients may provide a novel means for tumor detection. Such alterations are a major characteristic of many types of tumor especially those associated with head or neck cancer. Moreover, recent evidence suggests that senescent tumor cells release DNA into the circulation, which is subsequently carried by the blood and thus enriched in the serum and plasma. We tested 10 head and neck cancer patients (5 with malignant melanomas (MM) and 5 with adenoid cystic carcinomas (ACC)) by polymerase chain reaction (PCR)-based microsatellite analysis of DNA from white blood cells and paired plasma samples. Our goal was to amplify two microsatellite markers, D1S243 and D19S246, which sometimes show microsatellite alterations in head and neck cancer patients. However amplification of fragments from three loci in the plasma samples proved impossible, probably due to the small amounts of DNA isolated. We used multiple displacement amplification (MDA) to amplify genomic DNA from the plasma samples. Two microsatellite fragments were amplified from whole genome amplified DNA. Among 5 heterozygote samples, 3 showed the same pattern in DNA samples from both blood cells and plasma but 2 showed loss of heterozygosity (LOH). Although further study is necessary to confirm whether the LOH found in this study reflects alteration in circulating tumor cell DNA, application of whole genome amplification may allow DNA analysis from limited amounts of such DNA and provide a minimally invasive

diagnostic procedure and useful aid in therapy.

Key words: Malignant melanoma, Adenoid cystic carcinoma, Loss of heterozygosity (LOH), Plasma or serum DNA, Circulating tumor DNA

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