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ADDITION AND CORRECTION

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Correction to "Targeted Drug Delivery to Lymphocytes: A Route to Site-Specific Immunomodulation?"

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As part of ongoing programs in this area we recently had occasion to re-examine the data reported in this manuscript. In doing so we unfortunately identified a spreadsheet calculation error that affects the calculation of the extent of lymphatic transport of JWH015 in one treatment group. This submission seeks to redress that calculation error. The error does not change the principal findings or conclusions of the manuscript.

Error. In the original manuscript, there was an error in the calculation of the lymphatic transport and lymphocyte uptake of JWH015 after administration with 40 mg of oleic acid emulsified in 5.6 mL of 0.2% Tween 80 in saline. The error stems from omission of the volume term in a dose calculation.

Corrections. In Table 1 and Figure 2, the correct proportion of the JWH015 dose transported into the lymph and recovered in lymphocytes in the lymph after administration with 40 mg of oleic acid is 1.49 ± 0.22% and 0.05 ± 0.02%, respectively, resulting in a fraction (as a %) of drug in lymphocytes of 3.9 ± 1.4%. In Table 3, the correct mass of JWH015 transported into the lymph and in lymph lymphocytes after administration with 40 mg of oleic acid is 14.9 ± 2.2 μg and 0.5 ± 0.2 μg, respectively. Furthermore, in Table 3 the administration of JWH015 with 40 mg rather than 4 mg of oleic acid resulted in an increase in the mass of drug transported into the lymph of 9.4-fold and increases in mass of drug in lymph lymphocytes of 31.6-fold. We have repeated lymphatic transport experiments with JWH015 to confirm these corrections and have obtained consistent results.

Implications. The principal findings and conclusions of the manuscript are unchanged. For a range of drugs, enhancing lymphatic drug transport results in increased drug exposure to lymphocytes. In the case of JWH015, administration with a higher lipid dose (40 mg vs 4 mg of oleic acid) increases intestinal lymphatic transport and recovery in lymphocytes, albeit it to a lower extent than originally published. Notwithstanding this correction, the key data in Figures 4 and 5 are unchanged. Thus, when JWH015 is administered with higher (40 mg) rather than lower (4 mg) quantities of oleic acid, the increase in lymphocyte exposure resulting from increased lymphatic transport after administration of the higher lipid dose significantly increases immunomodulatory activity. Indeed this updated data suggests that, even for drugs where lymphatic transport is moderate, increases in targeting to the intestinal lymphatics and thus lymphocytes may provide a significant pharmacodynamic benefit. We apologize to the research community for any confusion that this may have caused.

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