College of
Pharmacy
WASHINGTON STATE UNIVERSITY
HEALTH SCIENCES SPOKANE

Potential Role of the Uridine Diphosphate Glycosyltransferase 3A Family in Tobacco Carcinogen Metabolism

Ana Vergara, PhD Candidate
Pharmaceutical Sciences
Lazarus Laboratory

Abstract

The UDP glycosyltransferase (UGT) family are phase II enzymes important in the metabolism of endogenous and exogenous substances, including steroids and a variety of different carcinogens and drugs. The UGT3A subfamily consists of UGTs 3A1 and 3A2, which may play a role in the detoxification of tobacco carcinogens. Preliminary studies demonstrate that the UGT3A enzymes are expressed in a variety of aerodigestive tract tissues and exhibit activity against polycyclic aromatic hydrocarbons (PAHs). In addition, Western blot analysis revealed two UGT3A1 splice variants (SV-1 and SV-2) with SV-1 well-expressed in liver and SV-2 expressed in jejunum, lung, and larynx. The estimated protein sizes of the two UGT3A1 variants were consistent with variants described in Ensemble and UniProt; these variants were confirmed by RT-PCR and direct sequencing that contained deletions of exon 2 and 7 (SV-1) and exon 7 (SV-2). Two novel UGT3A1 SVs (SV-3, SV-4) were also amplified when amplifying SV-2 in jejunum; SV-4 is deleted in exon 3 and both variants are also deleted in exons 4 and 7. Future studies will focus on determining UGT3A enzyme activities against tobacco carcinogens, the role of UGT3A1 SVs in regulating UGT3A1 enzyme activity, and the potential role of these enzymes in susceptibility for tobacco-related cancers.