Genotoxicity of acrylamide expressed via metabolic activation in CYP over-expressing human cells

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The recent finding that acrylamide (AA), a potent carcinogen, is formed in food during cooking raises concern for keeping human health. We previously examined the genotoxicity of AA and its metabolite glycidamide (GA) by using human lymphoblast TK6 cells, and concluded that AA is weakly, but GA is highly mutagenic compound, predominantly causing point mutations (Koyama, et al., 2006). Although AA is known to be metabolized to GA by CYP2E1, which did not work in rat liver S9. In the present study, we investigated the expression of genotoxicity of AA by using CYP over-expressing transgenic cells. Human lymphoblast AHH-1 cells originally have high CYP1A1 activity and h2E1v2 cells showing over-expreses CYP2E1 is a transgenic cell line based on AHH-1. Both cells exhibited weak genotoxic response to AA, but there was no significant difference among them. we also employed MCL-5 cell lines, which over-expressing five metabolic enzymes, such as CYP1A2, CYP2A3, CYP3A4, CYP2E1 and meEpoxide hydroxylase. MCL-5 cells significantly induced gene mutations after the treatment of AA. These results suggested two possibilities; 1) AA is changed to GA by other metabolic enzyme except CYP2E1, 2) Another different metabolites from AA contribute to the genotoxicity of AA in in vitro system. To clarify the possibility, we are now characterizing gene mutations and DNA-adducts induced by AA in MCL-5 cells.

Keywords: acrylamide; glycidamide; transgenic cell lines; genotoxicity; metabolic activation