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Synthesis and *in vitro* anticancer evaluation of some 4,6-diamino-1,3,5-triazine-2-carbohydrazides as Rad6 ubiquitin conjugating enzyme inhibitors

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Abstract— Series of 4-amino-6-(arylamino)-1,3,5-triazine-2-carbohydrazides **(3a-e)** and N'-phenyl-4,6-bis(arylamino)-1,3,5-triazine-2-carbohydrazides **(6a-e),** *for ease of readership, we will abbreviate our compound names as " new triazines",* have been synthesized, based on the previously reported Rad6B-inhibitory diamino-triazinylmethyl benzoate anticancer agents TZ9 and 4-amino-N'-phenyl-6-(arylamino)-1,3,5-triazine-2-carbohydrazides. Synthesis of the target compounds was readily accomplished in two steps from either *bis*-aryl/aryl biguanides via reaction of phenylhydrazine or hydrazinehydrate with key 4-amino-6-*bis*(arylamino)/(arylamino)-1,3,5-triazine-2-carboxylate intermediates. These new triazine derivatives were evaluated for their abilities to inhibit Rad6B ubiquitin conjugation and *in vitro* anticancer activity against several human cancer cell lines: ovarian (OV90 and A2780), lung (H1299and A549), breast (MCF-7 and MDA-MB231) and colon (HT29) cancer cells by MTS assays. All the 10 new triazines exhibited superior Rad6B inhibitory activities in comparison to selective Rad6 inhibitor TZ9 that was reported previously. Similarly, new triazines also showed better

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