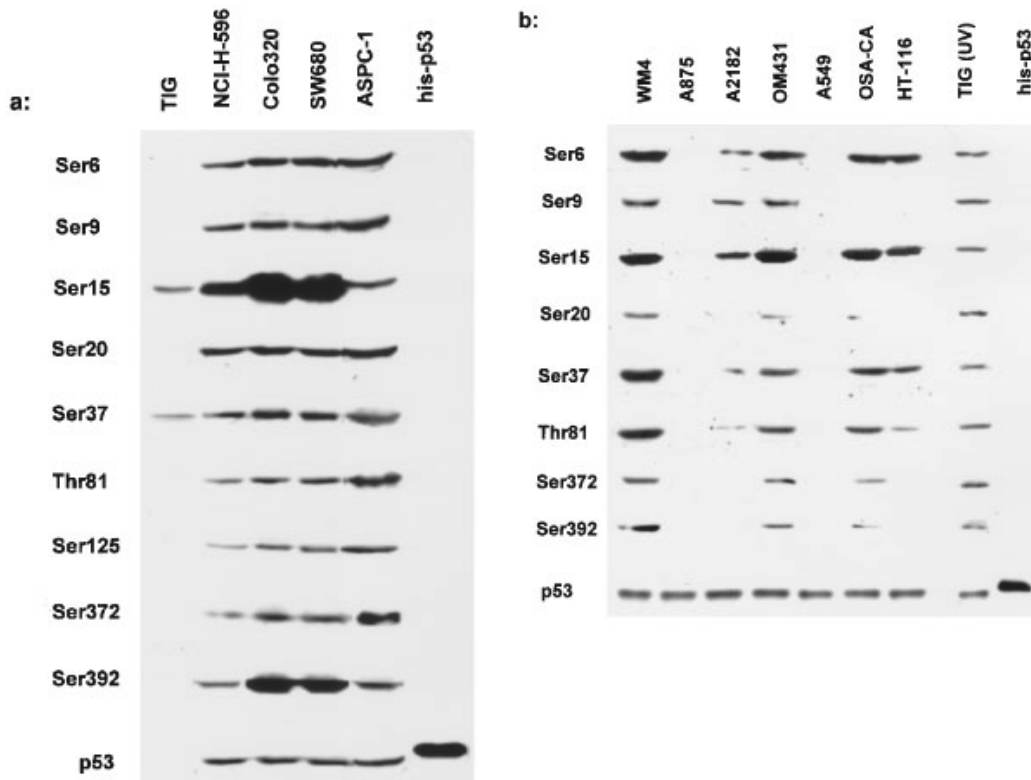


## Distinct pattern of p53 phosphorylation in human cancers

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The protein product of the tumor suppressor gene *p53* is phosphorylated on multiple residues by several protein kinases. The extensive changes seen in p53 phosphorylation during cell cycle progression led to the hypothesis that tumors may exhibit a different phosphorylation pattern of p53, either because of the presence of mutation, or deregulated kinases or phosphatases. Using a battery of 10 antibodies developed against different phosphorylated and acetylated residues of human p53 protein, we compared the pattern of p53 phosphorylation (at serines 6, 9, 15, 20, 37, 125, 372 and 392; threonine 81) and acetylation (at lysines 320/373/382) in tumor-derived cell lines, tumor samples, and non-neoplastic cells. Irrespective of tumor types or the presence of *p53* mutation, phosphorylation and acetylation of p53 was substantially higher in samples obtained from tumor cells and tissues than those found in non-transformed (non-neoplastic) samples (Figure). Among the 10 sites analyzed, phosphorylation of serines 15 and 392, and threonine 81, and acetylation at lysines 320/373/382 were among the more frequent modifications. Analysis of two of the more abundant phosphorylation or acetylation sites on p53 is sufficient to detect more than 70% of tumor-derived p53 protein samples. The distinct pattern of p53 phosphorylation and acetylation in human cancers may offer a new means to monitor the status and activity of p53 in the course of tumor development and progression.



**Figure.** Phosphorylation of mutant (a) and wt (b) p53 proteins in tumor-derived cell lines and normal human fibroblast (TIG) without and with UV irradiation, detected by Western blot analysis using antibodies specific to each phosphorylation sites. The amount of p53 protein in each sample was equal determined by labeling with anti-p53 antibody, pAb421. NCI-H596 (245<sup>Gly-Cys</sup>), lung adenosquamous carcinoma; Colo320 (248<sup>R-W</sup>), SW680 (273<sup>R-H</sup>), HT-116, colon adenocarcinoma; ASPC-1 (273<sup>R-H</sup>), pancreas adenocarcinoma; WM4, A875, A2182, OM431, A549, OSA-CA, malignant melanoma; his-p53, histidine-tagged recombinant wt p53 produced in bacteria.