

# A Novel Form of Parathyroid Hormone Found in Parathyroid Carcinoma with a Preserved N Terminus

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Until recently, it was assumed only one form of 1-84 PTH existed. However, our understanding of 1-84 PTH and the different PTH fragments has been limited by the "intact" PTH assay, which measures both 1-84 PTH and 7-84 PTH as well as other PTH fragments. We have developed both a novel 1-84 PTH (CAP) assay that detects PTH only if the first amino acid (serine) is present, and a total PTH (tPTH) assay that does not depend on the presence of the first serine. In normal subjects and in patients with both primary and secondary hyperparathyroidism, the level of tPTH is higher than that of CAP. Primary hyperparathyroid patients have tPTH levels 1.3-fold higher than CAP levels ( $132 \pm 14$  pg/mL vs  $96 \pm 10$  pg/mL). Thus, a substantial percentage of circulating PTH is in the form of large N-truncated fragments (likely 7-84 PTH). As parathyroid (PT) cancer is the most severe form of primary hyperparathyroidism, we were interested in the relationship between tPTH and CAP in two patients with metastatic parathyroid cancer: a male of 60 yrs, with a diagnosis of PT cancer for 26 years (Ca 13.4 mg/dL) and a female of 42 years with a diagnosis of PT cancer for 9 years (Ca 19.6 mg/dL; nl: 8.4-10.3). The male had CAP and tPTH levels of 946 and 797 pg/mL, respectively. The female had CAP and tPTH levels of 1619 and 1020 pg/mL, respectively. The fact that both patients had a higher level of CAP versus tPTH suggests that both patients have a novel form of PTH (nfPTH) that contains the first amino acid, serine. As both assays use the same capture antibody, the nfPTH is not an amino truncated fragment of PTH and has a length from 1 to at least the 44th amino acid, but may be a full-length or a large N terminal PTH fragment. In either case, post-translational phosphorylation/glycosylation or truncation may result in a unique three-dimensional fold that conceals the label antibody epitope for the tPTH assay. Further development of additional PTH assays should help elucidate nfPTH, leading to a better understanding of parathyroid cancer and the overall biology of the parathyroid gland.

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