

The role of PTH in mouse skin tumorigenesis

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Vitamin D and calcium are known to regulate differentiation and proliferation of keratinocytes; they may potentially have roles in suppressing carcinogenesis in squamous epithelium [1]. Indeed, the importance of the vitamin D receptor (VDR) in regulating cellular proliferation and differentiation was verified when the skin of mice lacking the VDR was reported to be susceptible to tumor formation [1]. In addition, knockout of the calcium sensing receptor in addition to VDR accelerated the development of skin tumors [2]. However, the role of Parathyroid Hormone (PTH) in tumorigenesis is yet to be elucidated. PTH is a classical endocrine hormone that was first identified more than 80 years ago as a key regulator of blood calcium levels [3]. Serum PTH is a sensitive indicator of calcium and vitamin D deficiency.

Recently it was reported that serum intact-PTH (iPTH) and a genetic polymorphism in *Pth* are important for skin tumor resistance [4]. Higher iPTH levels were detected in sera from cancer-resistant MSM/Ms mice compared with susceptible FVB/NJ mice. Skin carcinogenesis experiments with MSM-BAC transgenic mice (*Pth*^{MSM-Tg}) and *Pth* heterozygous knockout mice (*Pth*^{+/-}) showed the higher amounts of iPTH in sera conferred stronger resistance to skin tumors.

However, the differences was not detected in either serum calcium or 1,25(OH)₂D among MSM, *Pth*^{MSM-Tg} and *Pth*^{+/-} KO mice. These results indicate PTH confers resistance to skin tumors independently from serum calcium and vitamin D. In this report, it is also shown that PTH increases intracellular calcium in keratinocytes and promotes their terminal differentiation. Taken together, these data suggest that serum iPTH could serve as a prevention marker of skin cancer and a target for new therapies.

References

1. Zhang H, Lu H, Shrestha C, Feng Y, Li Y, et al. (2015) In serum, higher parathyroid hormone but not lower vitamin D is associated with oral squamous cell carcinoma. *Curr Oncol* 22: e259-e263. [[Crossref](#)]
2. Bikle DD (2011) The vitamin D receptor: a tumor suppressor in skin. *Discov Med* 11: 7-17. [[Crossref](#)]
3. Murray TM, Rao LG, Divieti P, Bringhurst FR (2005) Parathyroid hormone secretion and action: evidence for discrete receptors for the carboxyl-terminal region and related biological actions of carboxyl-terminal ligands. *Endocr Rev* 26: 78-11. [[Crossref](#)]
4. Okumura K, Saito M, Yoshizawa Y, Munakata H, Isogai E, et al. (2017) The parathyroid hormone regulates skin tumour susceptibility in mice. *Sci Rep* 11: 11208.

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