Cyclic AMP in neuroblastoma, ganglioneuroma and sympathetic ganglia

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Summary. Tissue content of cyclic AMP was as much as 10 times greater in ganglioneuroma than in neuroblastoma. This high cyclic AMP in ganglioneuroma was not significantly different from that of sympathetic ganglia.

The differentiation of neuroblastoma has been reported, both clinically and in vitro[1–4]. An elevation of cyclic adenosine 3′, 5′-monophosphate (cyclic AMP) has been confirmed to induce irreversibly several differentiated functions in cultured murine or human neuroblastoma cells[5]. In addition, it has also been suggested that the transformation of neuroblastoma cells to ganglioneuroma may be mediated by cyclic AMP[6]. At present it would be of great interest to determine whether cyclic AMP is actually deficient in neuroblastoma, and if it is significantly high in ganglioneuroma. We have assayed tissue levels of cyclic AMP in 7 mouse neuroblastoma Cl300, 10 human neuroblastomas, 3 ganglioneuromas and 4 human sympathetic ganglia which we present in this report.

Mouse neuroblastoma, weighing average 2 g, which developed 2–3 weeks after inoculation of tumor cells, was dissected from the s.c. area. Human tumors were surgically obtained from patients and sympathetic ganglia, 3 lumbar and 1 thoracic, were obtained at sympathectomy of patients with Buerger's and other related disease. For cyclic AMP assay, portions of all tissues were promptly frozen in liquid nitrogen. Other portions were histologically studied.

Frozen tissue was homogenized in cold 6% trichloroacetic acid. After centrifugation, the supernatant was acidified with HCl, extracted with ether. The aqueous phase was lyophilized and then dissolved in 50 mM acetate buffer, pH 4.0. Cyclic AMP was determined by Gilman's method[7] (Boehringer Mannheim GmbH Biochemica) and the trichloroacetate precipitable protein was determined according to the Lowry procedure[8]. The values were presented as pmoles of cyclic AMP per mg of protein. As shown in the table, it was found that cyclic AMP in neuroblastoma tissues, either human or mouse, was significantly lower ($p < 0.005$) than that in ganglioneuroma or sympathetic ganglia. The high cyclic AMP in ganglioneuroma was not significantly different from that of sympathetic ganglia. Cyclic AMP was as much as 10 times greater in ganglioneuroma than in neuroblastoma.

Specimens	n	cAMP (pmoles/mg protein) Range	Mean ± SD
Mouse neuroblastoma	7	0.8– 7.5	3.2 ± 2.2
Human neuroblastoma	10	1.5–12.8	5.3 ± 4.0
Human ganglioneuroma	3	28.5–54.5	39.9 ± 10.8
Human sympathetic ganglia	4	17.8–42.8	32.3 ± 9.1

These results indicate that neuroblastoma is a tumor with a relatively low level of cyclic AMP and again raises the question whether the correction of this condition would result in benign ganglioneuroma. Prasad et al.[9] proposed the new therapeutic approach, which aims at raising cyclic AMP level in tumor cells for the treatment of neuroblastoma. It was reported by them and others[6] that some agents, such as prostaglandin and/or phosphodiesterase inhibitor, were effective for that purpose. Our data provides a basis for such a therapeutic trial. A clinical evaluation of the effectiveness of the combined administration of PGE_1 and papaverine to patients with stage IV neuroblastoma is currently under study in our clinic.

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Elektronenmikroskopische Untersuchung am Übergangsepithel der Hausspitzmaus *(Crocidura russula)*[1]

Ultrastructural study of the transitional epithelium of the common European white-toothed shrew *(Crocidura russula)*

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Summary. The structure of the transitional epithelium of the common European white-toothed shrew (*Crocidura russula*) was examined by ultrathin serialsections. The epithelium consists of basal, intermediate and superficial cells. Basal and intermediate cells remain in contact with the basal lamina, whereas superficial cells have no connexion with the basal lamina.

Die bisher am ultradünnen Einzelschnitt oder an lichtmikroskopischen Serienschnitten erhobenen Befunde zur Schichtigkeit beziehungsweise Reihigkeit des Übergangsepithels sind bis heute widersprüchlich[2–4]. Petry und Amon[2] beschreiben das Übergangsepithel allgemein als

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