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DISSERTATION

**Studies in mice on the role of the thymic hormone thymulin during
early life as a maturational factor for the neuroendocrine system**

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Abbreviations

aa	amino acid
Ab	antibody
ABTS	2,2'-Azino-bis[3-ethylbenzothiazoline-6-sulfonic acid]
AVP	arginine vasopressin
BSA	bovine serum albumin
CD (4, 8)	cluster of differentiation (4, 8)
CD	cell density
CNS	central nervous system
CRP	C-reactive protein
CS	cell size
CVID	common variable immunodeficiency
DTNB	5,5'-Dithio-bis[2-nitrobenzoic acid]
ECM	extracellular matrix
EIA	enzyme immunoassay
ELISA	enzyme-linked immunosorbent assay
FCA	Freund's complete adjuvants
FIA	Freund's incomplete adjuvants
HRP	horseradish peroxidase
ICV	intracerebro-ventricular
i.c.	intracutaneous
i.d.	intra-dermal
IgG	immunoglobulin G
IgY	immunoglobulin Y (from egg yolk)
i.p.	intra-peritoneal
kDa	kilo Dalton
KLH	keyhole limpet hemocyanine
L-T	long-term (immunoneutralization)
MHC-I/II	major histocompatibility complex I/II
NHS	N-hydroxysuccinimide

OT	oxytocin
PBS	phosphate-buffered saline
PEG	polyethyleneglycol
POD	peroxidase
RA	rheumatoid arthritis
RIA	radioimmunoassay
rpm	revolutions per minute
RT	room temperature
s.c.	subcutaneous
SEM	standard error of the mean
SD	standard deviation
S-T	short-term immunoneutralization
TBS	tris-buffered saline
TdT	terminal deoxynucleotidyl transferase
TEC	thymic epithelial cells
TNC	thymic nurse cells
VD	volume density

Summary

The thymic peptide thymulin was discovered, purified and sequenced in the '70s. In a series of early studies, thymulin was thoroughly characterized in relation to its immunological actions. It was shown to be involved in several aspects of intra- and extrathymic T-cell differentiation. Further studies revealed that thymulin secretion was affected by a complex endocrine network involving most adenohypophyseal and peripheral hormones, and that thymulin itself strongly influences the neuroendocrine system.

In the present doctoral thesis anti-thymulin specific antibodies were generated in rabbits and chickens. An ELISA for thymulin was set up using mammalian antibodies. Rabbit antisera were specific for thymulin but chicken antibodies were found to produce strong nonspecific interactions when used in ELISA. Long- (33 days) and short- (7 days) term neonatal immunoneutralization studies on mice employing the anti-thymulin antibodies raised in rabbits revealed a strong reduction in the serum levels of most anterior pituitary hormones (LH, FSH, PRL, TSH and GH) when the treated animals reached an adult age. Pituitary cell populations were also affected by the treatment. Additionally, body weight decreased and thymic cellularity increased in the thymulin-deprived animals.

We conclude that thymulin has a general facilitatory action on anterior pituitary hormone secretion and that this thymic peptide plays a key role during early life for the development of a proper neuroendocrine balance in adult animals.

Zusammenfassung

Das thymische Peptid Thymulin wurde in den 70er Jahren entdeckt, purifiziert und sequenziert. In einer Reihe von Studien wurde Thymulin eingehend hinsichtlich seiner immunologischen Funktionen charakterisiert. Es wurde gezeigt, dass es an zahlreichen Aspekten intra- und extrathymischer T-Zell-Differenzierung beteiligt ist. Weitere Studien ergaben, dass die Sekretion von Thymulin durch ein komplexes Netzwerk gesteuert wird, an dem adenohipophysäre und periphere Hormone beteiligt sind, und dass Thymulin seinerseits sehr starken Einfluss auf das neuroendokrine System hat.

In der vorliegenden Doktorarbeit wurden anti-Thymulin-spezifische Antikörper in Kaninchen und Hühnern generiert. Ein ELISA für Thymulin wurde auf der Basis polyklonaler Kaninchenantikörper entwickelt. Kaninchenserum stellte sich als spezifisch für Thymulin heraus, wohingegen Hühnerantikörper starke unspezifische Interaktionen im ELISA zeigten. Neonatale Langzeit- (33 Tage) und Kurzzeit- (7 Tage) Immunoneutralisierungs-Studien in Mäusen führten nach Erreichen des Erwachsenenalters zu stark reduzierten Serumspiegeln adenohipophysärer Hormone (LH, FSH, PRL, TSH, GH). Die Morphologie hypophysärer Zellen zeigte in diesem Experiment ebenfalls Veränderungen. Außerdem waren in den Thymulin-defizienten Tieren das Körpergewicht erniedrigt und der Zellgehalt des Thymus erhöht.

Es kann gefolgert werden, dass Thymulin eine generelle sekretionsfördernde Wirkung auf die Adenohipophyse hat und dass dieses Peptid in der Neonatalperiode eine Schlüsselrolle für die normale Entwicklung des späteren neuroendokrinen Gleichgewichtes hat.

Curriculum Vitae

Mein Lebenslauf wird aus Datenschutzgründen in der elektronischen Version meiner Arbeit nicht mit veröffentlicht.

Lebenslauf

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Erklärung

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