Table I. Antioxidants and PUFA percentage in melanocytes cultures from 'low phototype' (LPM) and 'high phototype' (HPM) subjects[a]

	Vit. E, ng per 10^6 cells	SOD, U per 10^6 cells	Cat, U per 10^6 cells	Ratio, SOD per Cat	PUFA, % total fatty acids
LPM	4.10 ± 0.90	0.60 ± 0.21	0.25 ± 0.09	2.4	18.20 ± 1.20
HPM	2.55 ± 0.91*	0.55 ± 0.12	0.90 ± 0.18*	0.61*	12.90 ± 1.50*

[a]Each result represents the mean of two experiments in duplicate. *$p<0.001$.

Table II. Viability of melanocytes cultures from 'low phototype' (LPM) and 'high phototype' (HPM) subjects after treatment with CHU[a]

	0.66 μM	6.6 μM	20 μM
LPM	135 ± 10.0*	115 ± 4.5*	53 ± 4.1*
HPM	97.6 ± 4.2	96.2 ± 5.3	98.1 ± 6.6

[a]Cells were treated for 1 h in medium without fetal calf serum then washed and cultured in complete medium. Cell number was evaluated at 24 h by Trypan Blue test. Results are reported as percentage values compared with respective untreated controls and represent the mean ± SD of two experiments in triplicate. *$p<0.001$.

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Retardation of Hair Follicle Development by the Deletion of TrkC, High-Affinity Neurotrophin-3 Receptor

To the Editor:

Increasing evidence suggests that neurotrophins not only control neuronal development, plasticity, and maintenance (Lewin and Barde, 1996; Bothwell, 1997), but also are critically involved in the control of hair follicle (HF) development and growth (Holbrook *et al*, 1993; Crowley *et al*, 1994; Botchkarev *et al*, 1998a, 1999a).

Specifically, we have recently shown that neurotrophin-3 (NT-3) is functionally important for HF morphogenesis, as its overexpression or partial deletion in mice leads to a significant acceleration or retardation of HF development, respectively (Botchkarev *et al*, 1998a). As a member of the neurotrophin family, NT-3 shows multiple interactions with all types of neurotrophin receptors: NT-3 binds with high affinity to the tyrosine kinase C (TrkC) receptor, as well as with low affinity to the tyrosine kinase A (TrkA), tyrosine kinase B (TrkB), and p75 kDa neurotrophin receptor (p75NTR) (Lewin and Barde, 1996; Bothwell, 1997; Dechant and Barde, 1997).

Because all four receptors are expressed in the HF epithelium or mesenchyme during defined stages of HF morphogenesis (Botchkarev *et al*, 1998a),[1,2] the target receptor(s) that mediate the stimulatory effects of NT-3 on HF development are still unclear. TrkC, the high-affinity receptor for NT-3, is expressed by the hair placode epithelium during the initial steps of HF development, whereas in the fully developed HF TrkC expression appears in the dermal papilla, outer root sheath, and hair matrix (Botchkarev *et al*, 1998a). In order to explore the relative contribution of TrkC signaling in the control of HF, we have studied HF morphogenesis

Manuscript received May 3, 1999; accepted for publication May 28, 1999.

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[1]Botchkareva NV, Botchkarev VA, Peters EMJ, Paus R: Nerve growth factor and its receptors in murine skin: expression changes during hair follicle development and cycling. *Arch Derm Res* 290:71, 1998 (abstr.)

[2] Botchkarev VA, Lewin GR, Albers KM, Botchkareva NV, Peters EMJ, Paus R: Neurotrophins and murine hair follicle morphogenesis: expression patterns of NT-3, NT-4, brain-derived neurotrophic factor, TrkB and TrkC and indications for a functional role in hair follicle development and regression. *J Invest Dermatol* 108:620, 1997 (abstr.)

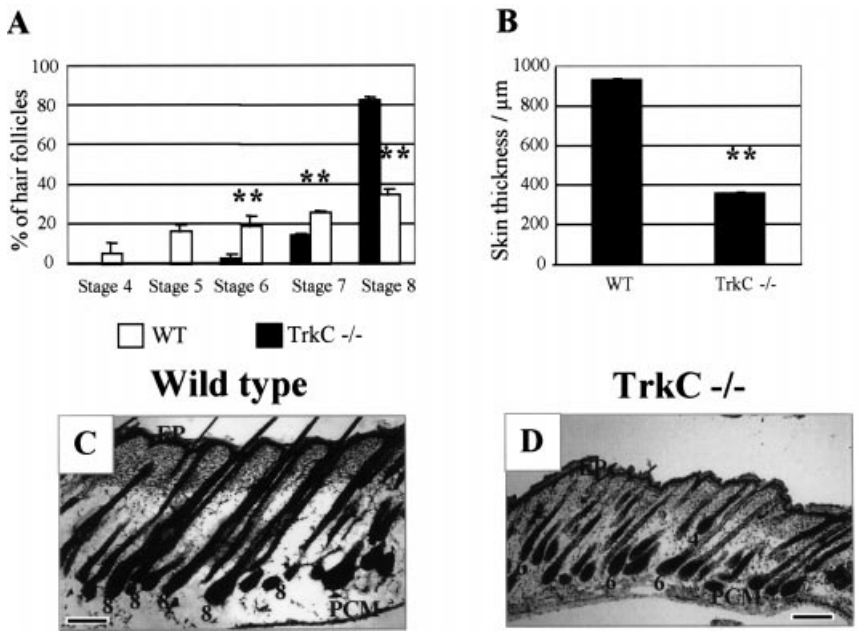

Figure 1. Retardation of hair follicle morphogenesis in TrkC knockout mice. The percentage of HF in defined stages of morphogenesis was evaluated by quantitative histomorphometry using established morphologic criteria in cryostat sections of the skin of TrkC knockout and wild-type mice at P5. (*A*) Dynamics of HF morphogenesis in TrkC knockout and wild-type mice show a presence of HF in stages 4–6 in TrkC knockout mice, a significant increase in the percentage of HF in stage 7 of HF morphogenesis, and a decline of HF at stage 8 in TrkC knockout mice, compared with wild-type animals. (*B*) Skin thickness in TrkC mutants is significantly declined at P5, compared with wild-type mice. (*C*, *D*) Representative skin examples of wild-type (*C*) and TrkC knockout mice (*D*) at P5. HF at different stages of development are indicated by arabic numbers. EP, epidermis; PCM, panniculus carnosus muscle. *Scale bars*: 200 µm.

in the back skin of TrkC knockout (–/–) mice, generated in a mixed background as described previously (Klein *et al*, 1994).

At day 5 of postnatal developments (P5), back skin of TrkC knockout (n = 3) and corresponding age-matched wild-type (n = 3) mice was dissected at the level of subcutis, immediately transferred to liquid nitrogen and embedded as described (Paus *et al*, 1994). Eight micrometer cryostat sections were prepared from frozen skin samples, and histochemical detection of endogenous alkaline phosphatase activity was performed to identify precisely the defined stages of HF morphogenesis (Handjiski *et al*, 1994). The percentage of HF in different stages of morphogenesis was assessed and calculated on the basis of accepted morphologic criteria (Paus *et al*, 1997; Philpott and Paus, 1998). Only every tenth cryosection was used for analysis in order to exclude the repetitive evaluation of the same HF, and 2–3 cryosections were assessed from each animal. A total of 150–350 follicles in 50–60 microscopic fields (approximately 50–60 follicles per animal) were analyzed and compared with that of a corresponding number of HF from the appropriate, age-matched wild-type mice. Thickness of skin was assessed as described before (Botchkarev *et al*, 1998b, 1999b). All sections were analyzed at ×200 magnification, and means and SEM were calculated from pooled data. Differences were judged as significant if the p value was < 0.05, as determined by independent Student's t test for unpaired samples. Photo-documentation was performed with the help of a digital image analysis system (ISIS METASYSTEMS, Altlussheim, Germany).

Comparative, quantitative histomorphometry (Botchkarev *et al*, 1998a) showed considerable, statistically significant differences in HF development between TrkC null mice and age-matched wild-type control. In contrast to wild-type mice, where all HF were in the latest stages of morphogenesis (6–8), TrkC mutants showed a dramatic retardation of HF development. This was evident by the predominance of stages 4–7 HF ($p < 0.005$), and the marked reduction in the number of stage 8 HF in TrkC null mice ($p < 0.005$) (**Fig 1*A*, *C*, *D***). Furthermore, as an important indirect indicator for a retarded HF development (Botchkarev *et al*, 1998a; Philpott and Paus, 1998), skin thickness in TrkC mutants was significantly lower ($p < 0.005$) than in wild-type mice (**Fig 1*B–D***).

Although the precise roles for other neurotrophin receptors (TrkA, TrkB, p75NTR) in the mediation of the effects of NT-3 on HF development remain to be elucidated, the current data fully corroborate our findings in NT-3 mutants (Botchkarev *et al*, 1998a), and suggest that NT-3 most likely stimulates HF morphogenesis via its high-affinity TrkC receptor. Recent observations in other models suggest that expression of NT-3 and TrkC are upregulated by Wnt- and BMP-family members (Kobayashi *et al*, 1988; Zhang *et al*, 1998; Patapoutian *et al*, 1999), which are shown to be critical for HF development (Philpott and Paus, 1998; Millar *et al*, 1999; Botchkarev *et al*, 1999c). Therefore, serving as a potential target for Wnt- and/or BMP-regulation, NT-3/TrkC signaling represents an important stimulatory component in the inductive signaling cascade driving HF morphogenesis.

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Animal Models of Psoriasis

To the Editor:

The review (Schön, 1999) of animal models in psoriasis does not convey the importance of microbial antigen in the transgenic HLA-B27 rat model. When delivered and raised under germ-free conditions those rats do not demonstrate Reiter syndrome-like changes in either their gut or their joints (Taurog *et al*, 1994). They do show skin and nail disease, but the authors speculate that those might be due to the presence of nonviable microorganisms in the sterile but not antigen-free environment of their cages.

Also, psoriasis-like lesions that include the feature of the Muno abscess can be induced in rabbits by a twice-daily topical application of heat-killed *Malassezia ovalis* antigen (Rosenberg *et al*, 1980; Xu *et al*, 1991).

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Manuscript received May 18, 1999; accepted for publication June 2, 1999.

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