

## STELLINGEN

behorende bij het proefschrift:

HUMAN GRANULOCYTE COLONY-STIMULATING FACTOR RECEPTOR:  
FUNCTION OF CYTOPLASMIC SUBDOMAINS AND RECEPTOR DEFECTS IN  
CONGENITAL NEUTROPENIA AND ACUTE MYELOID LEUKEMIA

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## I

It is of critical importance to investigate the maturation-signaling pathways of the G-CSF receptor. Insights into such signaling events will not only add to our understanding of the normal regulatory mechanisms of myeloid cell development, but also help unravel the pathophysiology of certain myeloid disorders, such as acute myeloid leukemia (AML) and neutropenias.

*This thesis*

## II

G-CSF has been successfully applied in the treatment of patients with severe congenital neutropenia (SCN). Nonetheless, alternative strategies of treatment need to be developed for SCN patients expressing G-CSF receptors with a C-terminal truncation.

*This thesis*

## III

Deregulated expression of c-Myc, a nuclear transcription factor that drives cell cycle progression, induces apoptosis in cells that are deprived of growth factors. The c-Myc-mediated apoptosis, however, does not result from the inappropriate activation of proliferative signaling by c-myc, as has been proposed in the "conflicting signal" theory.

*Cohen, Immunol. Today 14:126, 1993*

## IV

JAK2 kinase is not involved in the signaling pathway of IL-2. The 114-kDa "JAK2" protein that Tanaka *et al* reported to be physically associated with the  $\gamma_c$  chain of IL-2 receptor and activated following IL-2 stimulation is JAK3.

*Tanaka et al., Proc. Natl. Acad. Sci. USA 91:7271, 1994*

## V

The translocation t(15;17), which leads to the formation of PML-RAR $\alpha$  fusion oncoprotein, is the only chromosomal abnormality seen in the majority of cases of acute promyelocytic leukemia (APL). Nevertheless, this by no means implies that t(15;17) is all that is required for a full leukemic transformation.

*Grignani et al., Cell 74:423, 1994*

## VI

Dimerization of cytokine receptor components is essential but not sufficient for receptor activation.

## VII

In the majority of cases of myelodysplastic syndrome (MDS), the ineffective hematopoiesis is due, at least in part, to the premature apoptosis of hematopoietic progenitor cells.

## VIII

The primary action of the chimeric oncoprotein BCR-ABL, produced in chronic myelogenous leukemia (CML) as a consequence of translocation t(9;22), is to promote survival rather than proliferation of hematopoietic cells.

## IX

The human erythropoietin receptor (EPO-R) contains at least one additional as yet unidentified component that associates with the cloned EPO-R molecule.

## X

The translocation t(8;21)(q22;q22) juxtaposes the 5' portion of the *AML1* gene on chromosome 21 to nearly the entire *MTG/ETO* gene on chromosome 8, resulting in the production of AML-MTG/ETO fusion protein. The major leukemogenic event in this translocation is truncation of the AML1 protein rather than fusion of AML1 to the MTG/ETO.

