Regulation of cardiac form and function: small RNAs and large hearts

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Regulation of Cardiac Form and Function
small RNAs and large hearts

W.J. Wijnen
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Winandus Johannes Wijnen
**Front cover: Pythagoras Tree.** The Pythagoras Tree was first drawn by the Dutch mathematician Albert E. Bosman. It is the representation of a mathematical formula in which a triangle is placed to the side of a square, with the sides of the triangle forming the base for new squares. The algorithm can continue until infinity, but to draw this tree it was limited to 12 repetitions.

This Pythagoras Tree represents the quest for knowledge. Starting with an initial question (the central square), each answer (the triangles) gives rise to new questions (the subsequent squares). Answering questions therefore brings knowledge, but also raises new questions. The surface area of the tree represents knowledge and the perimeter represents the boundary with the unknown. Therefore, an increase in knowledge paradoxically creates an increased perception of the unknown.


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ACADEMISCH PROEFSCHRIFT

ter verkrijging van de graad van doctor
aan de Universiteit van Amsterdam
op gezag van de Rector Magnificus
prof. dr. D.C. van den Boom
ten overstaan van een door het College voor Promoties
ingestelde commissie,
in het openbaar te verdedigen in de Agnietenkapel
op donderdag 21 mei 2015, te 10:00 uur

door

Winandus Johannes Wijnen

geboren te Gulpen
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Faculteit der Geneeskunde
To the past, on which we build
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Preface

Investments in life science research hold the promise to improve disease treatment and preventive care, thereby increasing general health levels and life expectancy. A deeper understanding of the general and specific biological processes that underlie cellular (patho)physiology has already proven beneficial in the prevention and treatment of many, previously deadly, diseases. Sanitary improvements, vaccination, antibiotics and the cardiac pacemaker are among the abundant examples where insights in the disease mechanisms led to the reduction or eradication of previously common diseases. Consequently, this has resulted in a shift of the causes of mortality in the developed world from infectious diseases and acute events to more chronic diseases. Currently, the main causes of morbidity and mortality are represented by cancer, type II diabetes and chronic cardiovascular diseases like atherosclerosis, hypertension and heart failure. With increasing life expectancies and an ageing population, the need for treatment of these chronic diseases is increasing.

In the Netherlands cardiovascular diseases rank second among the general causes of mortality. As a whole its incidence has been decreasing over the period from 1991-2013 (1, 2). This decrease in mortality is however mainly due to better treatment of acute cardiovascular events and masks the shift towards chronic heart disease like heart failure (2). The ageing population also puts more people at risk to develop heart failure. Chronic cardiovascular disease and heart failure in particular therefore pose an increasing socio-economic burden to society, making prevention and treatment top priorities for research.

The research described in this thesis aims to provide better insights in the molecular biology underlying cardiac disease, and heart failure in particular. Hopefully some of these findings will eventually find their translation into clinical practice and contribute to improve patient care, while others provoke original thoughts that will stimulate additional research.

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The doctor provides immediate care for the individual patient
The scientist seeks knowledge to help many in the long run

It is however the synergy between the two that holds the key to successful disease treatment