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Allogeneic haematopoietic stem cell donation and transplantation across the MHC class I barrier: "Faster is better than more. More is better than less".

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ALLOGENEIC HAEMATOPOIETIC STEM CELL DONATION
AND TRANSPLANTATION
ACROSS THE MHC CLASS I BARRIER:

FASTER IS BETTER THAN MORE
MORE IS BETTER THAN LESS

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Martin Bartholomeus Alexander Heemskerk
geboren te Haarlem
in 1976

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Cover: The picture shows a pied crow sitting on a cannon above the entrance of the fortress at Cape Coast, Ghana. This fortress was notorious for its “door of no return” through which hundreds of thousands of Africans were forcefully loaded onto slave ships.

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**Aan mijn Opa Theo en Oma Gré
en mijn ouders Bart en Ada**

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Preface

This thesis describes the results of my attempt to help solving one of the major problems faced in haematopoietic stem cell transplantation, namely the lack of suitable stem cell donors. This problem has been around since the beginning of transplantation. Over the years a lot has changed for the better in the stem cell transplantation society and I personally think that it is time for a new scope.

As you will read in this thesis one of the ways to solve problems is to state that it is not a problem anymore and to just replace it by another obstacle. It seems like an easy way out, but it actually cost a lot of effort to discover that the size of the worldwide donor pool is no longer the biggest constraint for finding a suitable donor for patients waiting for a graft. Unfortunately, this is not true for patients of non-Northwest European origin. For these patients the number one solution remains to be the increase of their donor pool or in other words developing the underdeveloped countries.

For the patients without a suitable donor I tried to define general rules for acceptable histocompatibility mismatches. This idea of acceptable mismatches originated from past observations of patients having received a graft with a major mismatch, which surprisingly enough did not hamper successful transplantation. It seems contradictory to put words like histocompatibility and acceptable mismatches in the same sentence without mentioning good fortune. However, my proposed definition of acceptable mismatches gives the impression of being even more contradictory. It is certainly not the most obvious one and goes against one of the primary beliefs in transplantation.

This new scope however is accompanied by its own challenges. The first of which is that we actually did not solve the problem but only redefined it. This implies that this study is still in progress and thus creates new research opportunities. The second challenge is accurately stated by Niccolò Machiavelli in his *Il Principe*: “And it ought to be remembered that there is nothing more difficult to take in hand, more perilous to conduct, or more uncertain in its success, than to take the lead in the introduction of a new order of things. Because the innovator has for enemies all those who have done well under the old conditions and lukewarm defenders in those who may do well under the new. This coolness arises partly from fear of the opponents, who have the laws on their side, and partly from the incredulity of men, who do not readily believe in new things until they have had a long experience of them. Thus it happens that whenever those who are hostile have the opportunity to attack they do it like partisans, whilst the others defend lukewarmly, in such wise that the prince is endangered along with them.” Fortunately, I was in good company.

In the hope that you may find this thesis appealing,

Martin Heemskerck