Cover Page



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Mismatch repair and MUTYH deficient colorectal cancers: at the crossroad of genomic stability and immune escape

Noel Filipe da Cunha Carvalho de Miranda

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Mismatch repair and MUTYH deficient colorectal cancers: at the crossroad of genomic stability and immune escape

Proefschrift

ter verkrijging van de graad van Doctor aan de Universiteit Leiden, op gezag van Rector Magnificus prof.mr. C.J.J.M. Stolker, volgens besluit van het College voor Promoties te verdedigen op dinsdag 19 November 2013 klokke 10.00 uur

door

Noel Filipe da Cunha Carvalho de Miranda geboren te Póvoa de Varzim, Portugal in 1982

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Kettlewell found that in unpolluted areas, more of his light-colored moths had survived. In soot-blacked areas, more of the dark-colored moths had survived. Thus Kettlewell showed that in each environment the moths that were better camouflaged had the higher survival rate. It was logical to conclude that when soot darkened the tree trunks in the area, natural selection caused the dark-colored moths to become more common. Today Kettlewell's work is considered to be a classic demonstration of natural selection in action.

-BIOLOGY ("The Elephant Book"), Miller & Levine, p.298. -

To my parents and in memory of Prof. Noé Gonçalves de Miranda

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Abbreviations:

BMP Bone morphogenetic protein CIMP CpG island methylator phenotype

CIN Chromosomal instability

CTL Cytotoxic T cell

FAP Familial adenomatous polyposis HLA Human leukocyte antigen

HNPCC Hereditary non-polyposis colorectal cancer

MAP MUTYH-associated polyposis MHC Major histocompatibility complex

MSI Microsatellite instability
MSI-H Microsatellite instability - high

NK Natural killer

TGF-β Transforming growth factor beta