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Germline variants in the mismatch repair genes: Detection and phenotype

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LIST OF PUBLICATIONS

An alternative approach to establishing unbiased colorectal cancer risk estimation in Lynch syndrome.

Suerink M, Rodriguez-Girondo M, van der Klift HM, Colas C, Brugieres L, Lavoine N, Jongmans M, Munar GC, Evans DG, Farrell MP, Genuardi M, Goldberg Y, Gomez-Garcia E, Heinimann K, Hoell JI, Aretz S, Jasperson KW, Kedar I, Modi MB, Nikolaev S, van Os TAM, Ripperger T, Rueda D, Senter L, Sjursen W, Sunde L, Therkildsen C, Tibiletti MG, Trainer AH, Vos YJ, Wagner A, Winship I, Wimmer K, Zimmermann SY, Vasen HF, van Asperen CJ, Houwing-Duistermaat JJ, Ten Broeke SW, Nielsen M. *Genetics in Medicine*. 2019;21(12):2706-2712.

Constitutional mismatch repair deficiency as a differential diagnosis of neurofibromatosis type 1: consensus guidelines for testing a child without malignancy.

Suerink M, Ripperger T, Messiaen L, Menko FH, Bourdeaut F, Colas C, Jongmans M, Goldberg Y, Nielsen M, Muleris M, van Kouwen M, Slavc I, Kratz C, Vasen HF, Brugieres L, Legius E, Wimmer K. *Journal of Medical Genetics*. 2019;56(2):53-62.

Constitutional mismatch repair deficiency in a healthy child: On the spot diagnosis?

Suerink M, Potjer TP, Versluijs AB, Ten Broeke SW, Tops CM, Wimmer K, Nielsen M. *Clinical Genetics*. 2018;93(1):134-137.

The effect of genotypes and parent of origin on cancer risk and age of cancer development in PMS2 mutation carriers.

Suerink M, van der Klift HM, Ten Broeke SW, Dekkers OM, Bernstein I, Capella Munar G, Gomez Garcia E, Hoogerbrugge N, Letteboer TG, Menko FH, Lindblom A, Mensenkamp A, Moller P, van Os TA, Rahner N, Redeker BJ, Olderode-Berends MJ, Spruijt L, Vos YJ, Wagner A, Morreau H, Hes FJ, Vasen HF, Tops CM, Wijnen JT, Nielsen M. *Genetics in Medicine*. 2016;18(4):405-409.

Findings Linking Mismatch Repair Mutation With Age at Endometrial and Ovarian Cancer Onset in Lynch Syndrome.

Suerink M, Ten Broeke SW, Nielsen M. *JAMA Oncol*. 2018;4(6):889-890.

Prevalence of mismatch repair deficiency and Lynch syndrome in a cohort of unselected small bowel adenocarcinomas.

Suerink M, Kilinc G, Terlouw D, Hristova H, Sensuk L, van Egmond D, Farina Sarasqueta A, Langers AMJ, van Wezel T, Morreau H, Nielsen M, collaborators PA-g.

Published online ahead of print in Journal of Clinical Pathology. 2020. doi: 10.1136/jclinpath-2020-207040.

Report of the fifth meeting of the European Consortium 'Care for CMMRD' (C4CMMRD), Leiden, The Netherlands, July 6th 2019.

Suerink M, Wimmer K, Brugieres L, Colas C, Gallon R, Ripperger T, Benusiglio PR, Bleiker EMA, Ghorbanoghli Z, Goldberg Y, Hardwick JCH, Kloor M, le Mentec M, Muleris M, Pineda M, Ruiz-Ponte C, Vasen HFA.

Familial Cancer. 2020.

The Apparent Genetic Anticipation in PMS2-Associated Lynch Syndrome Families Is Explained by Birth-cohort Effect.

Ten Broeke SW, Rodriguez-Gironde M, Suerink M, Aretz S, Bernstein I, Capella G, Engel C, Gomez-Garcia EB, van Hest LP, von Knebel Doeberitz M, Lagerstedt-Robinson K, Letteboer TGW, Moller P, van Os TA, Pineda M, Rahner N, Olderde-Berends MJW, von Salome J, Schackert HK, Spruijt L, Steinke-Lange V, Wagner A, Tops CMJ, Nielsen M.

Cancer Epidemiology, Biomarkers and Prevention. 2019;28(6):1010-1014.

Cancer Risks for PMS2-Associated Lynch Syndrome.

Ten Broeke SW, van der Klift HM, Tops CMJ, Aretz S, Bernstein I, Buchanan DD, de la Chapelle A, Capella G, Clendenning M, Engel C, Gallinger S, Gomez Garcia E, Figueiredo JC, Haile R, Hampel HL, Hopper JL, Hoogerbrugge N, von Knebel Doeberitz M, Le Marchand L, Letteboer TGW, Jenkins MA, Lindblom A, Lindor NM, Mensenkamp AR, Moller P, Newcomb PA, van Os TAM, Pearlman R, Pineda M, Rahner N, Redeker EJW, Olderde-Berends MJW, Rosty C, Schackert HK, Scott R, Senter L, Spruijt L, Steinke-Lange V, Suerink M, Thibodeau S, Vos YJ, Wagner A, Winship I, Hes FJ, Vasen HFA, Wijnen JT, Nielsen M, Win AK.

Journal of Clinical Oncology. 2018;36(29):2961-2968.

List of publications

Declining detection rates for APC and biallelic MUTYH variants in polyposis patients, implications for DNA testing policy.

Terlouw D, [Suerink M](#), Singh SS, Gille H, Hes FJ, Langers AMJ, Morreau H, Vasen HFA, Vos YJ, van Wezel T, Tops CM, Ten Broeke SW, Nielsen M.

European Journal of Human Genetics. 2020;28(2):222-230.

High-sensitivity microsatellite instability assessment for the detection of mismatch repair defects in normal tissue of biallelic germline mismatch repair mutation carriers.

Gonzalez-Acosta M, Marin F, Puliafito B, Bonifaci N, Fernandez A, Navarro M, Salvador H, Balaguer F, Iglesias S, Velasco A, Grau Garces E, Moreno V, Gonzalez-Granado LI, Guerra-Garcia P, Ayala R, Florkin B, Kratz C, Ripperger T, Rosenbaum T, Januszkiewicz-Lewandowska D, Azizi AA, Ragab I, Nathrath M, Pander HJ, Lobitz S, [Suerink M](#), Dahan K, Imschweiler T, Demirsoy U, Brunet J, Lazaro C, Rueda D, Wimmer K, Capella G, Pineda M.

Journal of Medical Genetics. 2020;57(4):269-273.

Lynch syndrome caused by germline PMS2 mutations: delineating the cancer risk.

ten Broeke SW, Brohet RM, Tops CM, van der Klift HM, Velthuizen ME, Bernstein I, Capella Munar G, Gomez Garcia E, Hoogerbrugge N, Letteboer TG, Menko FH, Lindblom A, Mensenkamp AR, Moller P, van Os TA, Rahner N, Redeker BJ, Sijmons RH, Spruijt L, [Suerink M](#), Vos YJ, Wagner A, Hes FJ, Vasen HF, Nielsen M, Wijnen JT.

Journal of Clinical Oncology. 2015;33(4):319-325.

Molecular Background of Colorectal Tumors From Patients With Lynch Syndrome Associated With Germline Variants in PMS2.

Ten Broeke SW, van Bavel TC, Jansen AML, Gomez-Garcia E, Hes FJ, van Hest LP, Letteboer TGW, Olderode-Berends MJW, Ruano D, Spruijt L, [Suerink M](#), Tops CM, van Eijk R, Morreau H, van Wezel T, Nielsen M.

Gastroenterology. 2018;155(3):844-851.

No Overt Clinical Immunodeficiency Despite Immune Biological Abnormalities in Patients With Constitutional Mismatch Repair Deficiency.

Tesch VK, H IJ, Raicht A, Rueda D, Dominguez-Pinilla N, Allende LM, Colas C, Rosenbaum T, Ilcencikova D, Baris HN, Nathrath MHM, [Suerink M](#), Januszkiewicz-Lewandowska D, Ragab I, Azizi AA, Wenzel SS, Zschocke J, Schwinger W, Kloor M, Blattmann C, Brugieres L, van der Burg M, Wimmer K, Seidel MG.

Frontiers in Immunology. 2018;9:1506.

Patients with High-Grade Gliomas and Cafe-au-Lait Macules: Is Neurofibromatosis Type 1 the Only Diagnosis?

Guerrini-Rousseau L, [Suerink M](#), Grill J, Legius E, Wimmer K, Brugieres L.
AJNR: American Journal of Neuroradiology. 2019;40(6):E30-E31.

Putting genome-wide sequencing in neonates into perspective.

van der Sluijs PJ, Aten E, Barge-Schaapveld D, Bijlsma EK, Bokenkamp-Gramann R, Donker Kaat L, van Doorn R, van de Putte DF, van Haeringen A, Ten Harkel ADJ, Hilhorst-Hofstee Y, Hoffer MJV, den Hollander NS, van Ierland Y, Koopmans M, Kriek M, Moghadasi S, Nibbeling EAR, Peeters-Scholte C, Potjer TP, van Rij M, Ruivenkamp CAL, Rutten JW, Steggerda SJ, [Suerink M](#), Tan R, van der Tuin K, Visser R, van der Werf-
't Lam AS, Williams M, Witlox R, Santen GWE.
Genetics in Medicine. 2019;21(5):1074-1082.

Recurrent APC Splice Variant c.835-8A>G in Patients With Unexplained Colorectal Polyposis Fulfilling the Colibactin Mutational Signature.

Terlouw D, [Suerink M](#), Boot A, van Wezel T, Nielsen M, Morreau H.
Gastroenterology. 2020.

Repertoire Sequencing of B Cells Elucidates the Role of UNG and Mismatch Repair Proteins in Somatic Hypermutation in Humans.

H IJ, van Schouwenburg PA, Pico-Knijnenburg I, Loeffen J, Brugieres L, Driessen GJ, Blattmann C, [Suerink M](#), Januszkiewicz-Lewandowska D, Azizi AA, Seidel MG, Jacobs H, van der Burg M.
Frontiers in Immunology. 2019;10:1913.

Response to Roberts et al. 2018: is breast cancer truly caused by MSH6 and PMS2 variants or is it simply due to a high prevalence of these variants in the population?

Ten Broeke SW, [Suerink M](#), Nielsen M.
Genetics in Medicine. 2019;21(1):256-257.

List of publications

A sensitive and scalable microsatellite instability assay to diagnose constitutional mismatch repair deficiency by sequencing of peripheral blood leukocytes.

Gallon R, Muhlegger B, Wenzel SS, Sheth H, Hayes C, Aretz S, Dahan K, Foulkes W, Kratz CP, Ripperger T, Azizi AA, Baris Feldman H, Chong AL, Demirsoy U, Florkin B, Imschweiler T, Januszkiewicz-Lewandowska D, Lobitz S, Nathrath M, Pander HJ, Perez-Alonso V, Perne C, Ragab I, Rosenbaum T, Rueda D, Seidel MG, Suerink M, Taeubner J, Zimmermann SY, Zschocke J, Borthwick GM, Burn J, Jackson MS, Santibanez-Koref M, Wimmer K.

Human Mutation. 2019;40(5):649-655.

SNP association study in PMS2-associated Lynch syndrome.

Ten Broeke SW, Elsayed FA, Pagan L, Olderode-Berends MJW, Garcia EG, Gille HJP, van Hest LP, Letteboer TGW, van der Kolk LE, Mensenkamp AR, van Os TA, Spruijt L, Redeker BJW, Suerink M, Vos YJ, Wagner A, Wijnen JT, Steyerberg EW, Tops CMJ, van Wezel T, Nielsen M.

Familial Cancer. 2018;17(4):507-515.

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CURRICULUM VITAE

Manon was born in Rijswijk, the Netherlands, on February 11th 1991. In 2010 she graduated cum laude at her high school Gymnasium Juvenaat in Bergen op Zoom.

From July 2007 until May 2008 she participated in a high school exchange program, living with a host family and attending high school in Australia.

Manon started medical school in September 2010 at the Leiden University Medical Centre (LUMC) and graduated in 2016. During her medical education (in 2012) she joined the research group of Maartje Nielsen at the department of clinical genetics at the LUMC, at first as a student assistant to work on database management. Later on this turned into a research internship and her first scientific publication on the effect of genotype and parent-of-origin on the phenotype of *PMS2* carriers. After graduating medical school, she started as a PhD student combined with a part-time appointment as a resident (not in training) of clinical genetics. In January 2018 she started her training to become a clinical geneticist. This training was interrupted for 9 months from April 2018 onwards to work on research related to her PhD as well as research on *APC* mosaicism. Manon is actively involved in the European consortium 'Care for CMMRD' (C4CMMRD), which provides a platform to collaborate on research concerning constitutional mismatch repair deficiency. She will also join the European Reference Network (ERN) Genturis on the topic of CMMRD.