

Erasmus University Rotterdam, the Netherlands
CSC PhD 2015 Project Description

School/Department:	Erasmus MC Rotterdam, Department of Surgery Research group: RE search P rojects for Ab dominal surgery I nnovation R otterdam (REPAIR) Prof. J.F. Lange, Prof. J. Jeekel, and Prof. G.J Kleinrensink
Project Title:	The role of macrophages in surgical complications.
Abstract:	<p>Macrophages are key components of tissue repair and remodelling during wound healing. Classically activated macrophages, or M1 macrophages, propagate pro-inflammatory responses by producing cytokines such as interleukin (IL)-1b, tumor necrosis factor (TNF)-a and interleukin (IL)-6. Another subtype of macrophages is represented by the alternatively activated macrophages, or M2 macrophages. These cells arise when exposed to, for example, IL-4 or immune complexes. M2 macrophages produce among others IL-10 and chemokines CCL18 and CCL22 (i.e. macrophage derived chemokine) and are able to produce growth factors, promoting angiogenesis and extracellular matrix production.</p> <p>Despite the understanding of macrophage derivation, the crucial role of macrophages in postoperative complications are not discovered until the recent decades. Our group has been focusing on this topic to develop different strategies that may facilitate the prevention, diagnosis and treatment of different important surgical complications such as anastomotic leakage, postoperative ileus, incisional hernia, and wound complications after hernia mesh repair.</p> <p>Colorectal anastomotic leakage is still a significant problem in the field of colorectal surgery, occurring in 8% to 20% of patients and causing a mortality rate as high as 33%. Our research group is leading the experimental research on anastomotic leakage worldwide. One important part of research on the prevention of anastomotic leakage is to apply tissue adhesives on the anastomosis. Several ideal tissue adhesives have been selected based on our previous ex-vivo, in-vitro and in-vivo rodent studies. Polarization of the different macrophages play an important role in the healing of the anastomosis. The future experiments will focus on porcine tests and subsequently human application and the role of macrophages related to inflammation, tissue repair and remodelling. The PhD fellow will also participate these innovative projects to initiate the first human trials.</p> <p>Biocompatibility of implanted medical devices like mesh in hernia</p>

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	<p>repair is determined by the host foreign body reaction to the surface of the implanted material. The eventual success of an implantable medical device is strongly dependent on the response of the macrophages. Macrophages appear to possess remarkable plasticity once activated. We developed a culture model with human primary macrophages to evaluate the acute response of macrophages to biomaterials. With this culture model we get more insight in the foreign body reaction. In our on-going studies we aim to develop a culture model that can be used to test patient's own cells prior to surgery to give the best personal advise which mesh should be used. Additionally, we intend to have a close look to the foreign body reaction to tissue adhesives and suture materials in this culture model. This will be the next step which can be initiated by the PhD fellow.</p> <p>Another common complication after abdominal surgery is postoperative ileus (POI), a transit cessation of bowel mobility after surgery. It occurs in almost all the surgical patients and presents as an inability to tolerate enteral nutrition, associated with nausea, abdominal distension, and lack of flatus and defecation. One part of the pathophysiology is the inflammatory response to intestinal manipulation and trauma. In this phase, local macrophages, activated by intestinal manipulation, induce an inflammatory response that results in muscle dysfunction, and induce the infiltration of different inflammatory cells, especially the neutrophil infiltration into the intestinal muscularis. Therefore, systematic inflammatory markers, such as interleukine-1, interleukine-6 (IL-6), TNF- α and CRP, might be valuable for the early detection of POI. However, the correlation of these parameters and POI are still not yet demonstrated, thus more detailed data are still in great need. We have several projects on-going on this specific problem. The PhD fellow will also participate in these studies and can initiate a large randomized clinical study.</p>
Requirements of candidate:	<p>Master degree: Yes</p> <p>Background: a master-degree (or a bachelor-degree) in Medicine or Biology. Background in surgery/neuroscience is preferred.</p> <p>IELTS Grade: 7.0 (<i>minimal 6.0 per component</i>) or TOEFL: 100 (<i>minimal 20 per component</i>)</p>

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<p>Supervisor information:</p>	<p>Professor Lange (professor in surgery), Professor Jeekel (professor in surgery), and Professor Kleinrensink (professor in anatomy and neuroscience) are principal investigators and directors of the REPAIR research group. They supervise the PhD-projects of 7 fulltime PhD-fellows and more than 20 part-time research fellows.</p> <p>j.lange@erasmusmc.nl j.jeel@erasmusmc.nl g.kleinrensink@erasmusmc.nl</p> <p>Publication list:</p> <p>Deerenberg EB, Mulder IM, Grotenhuis N, Ditzel M, Jeekel J, Lange JF. Experimental study on synthetic and biological mesh implantation in a contaminated environment. Br J Surg. 2012 Dec;99(12):1734-41. doi: 10.1002/bjs.8954.</p> <p>Ditzel M, Deerenberg EB, Grotenhuis N, Harlaar JJ, Monkhurst K, Bastiaansen-Jenniskens YM, Jeekel J, Lange JF. Biologic meshes are not superior to synthetic meshes in ventral hernia repair: an experimental study with long-term follow-up evaluation. Surg Endosc. 2013 Oct;27(10):3654-62. doi: 10.1007/s00464-013-2939-y. Epub 2013 Apr 3.</p> <p>Grotenhuis N, Vd Toom HF, Kops N, Bayon Y, Deerenberg EB, Mulder IM, van Osch GJ, Lange JF, Bastiaansen-Jenniskens YM. In vitro model to study the biomaterial-dependent reaction of macrophages in an inflammatory environment. Br J Surg. 2014 Jul;101(8):983-92.</p> <p>Grotenhuis N, Bayon Y, Lange JF, Van Osch GJ, Bastiaansen-Jenniskens YM. A culture model to analyze the acute biomaterial-dependent reaction of human primary macrophages. Biochem Biophys Res Commun. 2013 Mar 29;433(1):115-20.</p> <p>Slieker, J. C., K. A. Vakalopoulos, N. A. Komen, J. Jeekel and J. F. Lange. "Prevention of Leakage by Sealing Colon Anastomosis: Experimental Study in a Mouse Model." J Surg Res 184, no. 2 (2013): 819-24.</p> <p>Vakalopoulos, K. A., F. Daams, Z. Wu, L. Timmermans, J. J. Jeekel, G. J. Kleinrensink, A. van der Ham and J. F. Lange. "Tissue Adhesives in Gastrointestinal Anastomosis: A</p>
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	<p>Systematic Review." J Surg Res 180, no. 2 (2013): 290-300.</p> <p>Vakalopoulos, K. A., Z. Wu, L. Kroese, G. J. Kleinrensink, J. Jeekel, R. Vendamme, D. Dodou and J. F. Lange. "Mechanical Strength and Rheological Properties of Tissue Adhesives with Regard to Colorectal Anastomosis: An Ex Vivo Study." Ann Surg, (2014).</p> <p>Zhouqiao Wu, Geesien S.A. Boersema, Leonard F. Kroese, Diman Taha, Sandra Vennix, Yvonne M. Bastiaansen-Jenniskens, King H. Lam, Maikel Peppelenbosch, Johannes Jeekel, Johan F. Lange Reducing colorectal anastomotic leakage with tissue adhesive in an experimental inflammatory bowel disease model, submitted</p> <p>Z. Wu, G.S.A. Boersema, L.F. Kroese, Van Neck, Lam, G.J. Kleinrensink, J. Jeekel, J.F. Lange. Improvement of anastomotic healing by Hyperbaric Oxygen Therapy (HBOT), submitted</p> <p>Z. Wu, K. A. Vakalopoulos, G. S. A. Boersema, K. Lam, Y.M. Bastiaansen-Jenniskens, G. J. Kleinrensink, J. Jeekel, J. F. Lange. The prevention of colorectal anastomotic leakage with tissue adhesives in a contaminated environment is associated with the presence of anti-inflammatory macrophages. International Journal of Colorectal Disease (accepted)</p> <p>Wu, Z., G. S. Boersema, K. A. Vakalopoulos, F. Daams, C. L. Sparreboom, G. J. Kleinrensink, J. Jeekel and J. F. Lange. "Critical Analysis of Cyanoacrylate in Intestinal and Colorectal Anastomosis." J Biomed Mater Res B Appl Biomater 102, no. 3 (2014): 635-42.</p> <p>Wu, Z., F. Daams, G. S. A. Boersema, J. Jeekel and J. F. Lange. "A Rat Model of Anastomotic Leakage Created by Insufficient Sutures after Partial Colectomy." In British journal of surgery, 100, 211-211: WILEY-BLACKWELL 111 RIVER ST, HOBOKEN 07030-5774, NJ USA, 2013.</p> <p>Wu, Z., F. Daams, G. S. A. Boersema, K. Vakalopoulos, K. Lam, P. van der Horst, Gert-Jan Kleinrensink, Johannes Jeekel and Johan Lange. "Colorectal Anastomotic Leakage Caused by Insufficient Suturing after Partial Colectomy: A</p>
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	<p>New Experimental Model." Surgical Infection, (2014): Accepted article.</p> <p>Wu, Z., K. A. Vakalopoulos, G. S. A. Boersema, J. Jeekel and J. F. Lange. "Prevention of Anastomotic Leakage with Tissue Adhesives in Contaminated Environment." In British journal of surgery, 100, 5-5: WILEY-BLACKWELL 111 RIVER ST, HOBOKEN 07030-5774, NJ USA, 2013.</p> <p>Wu, Z., K. A. Vakalopoulos, L. F. Kroese, G. S. Boersema, G. J. Kleinrensink, J. Jeekel and J. F. Lange. "Reducing Anastomotic Leakage by Reinforcement of Colorectal Anastomosis with Cyanoacrylate Glue." Eur Surg Res 50, no. 3-4 (2013): 255-61.</p> <p>Wu, Zhouqiao, Geesien S. A. Boersema, Konstantinos A. Vakalopoulos, Freek Daams, Cloe L. Sparreboom, Gert- Jan Kleinrensink, Johannes Jeekel and Johan F. Lange. "Critical Analysis of Cyanoacrylate in Intestinal and Colorectal Anastomosis." Journal of Biomedical Materials Research Part B: Applied Biomaterials 102, no. 3 (2014): 635-642.</p>
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