Hope for effective ulcerative colitis treatment

Ulcerative colitis, a chronic form of inflammatory bowel disease, is characterised by a reduced amount of the lipid phosphatidylcholine in the colon mucosa. This fact was discovered by Wolfgang Stremmel and his team at the University Hospital of Heidelberg. In collaboration with the Heidelberg-based biotechnology company Lipid Therapeutics, the researchers are now working on the development of a phosphatidylcholine drug for the treatment of this disease. In a further collaboration with the Freiburg-based company Dr. Falk Pharma, the drug is being brought to industrial maturity.

Ulcerative colitis is a chronic inflammatory disease of the colon which frequently occurs during adolescence or in young adults. The number of people with this disease is growing; in Germany around 170,000 to 200,000 people suffer from ulcerative colitis and on the global level, this number exceeds 1 million. Typical symptoms of the disease are inflammations of the intestinal mucosa, leading to characteristic ulcers and open sores in the colon, associated with diarrhoea mixed with blood, all symptoms which are often very painful. People who suffer from ulcerative colitis have to live with uncontrolled nightly bowel movements, which can occur from five to 30 times during the night/day. This has a serious effect on sufferers' professional and personal lives. The disease always starts in the rectum and then gradually spreads into the colon. Once the entire colon is affected, the disease is also referred to as ulcerative pancolitis, which carries an elevated risk of developing colon cancer. Ulcerative colitis is an intermittent disease characterised by periods of exacerbated symptoms and periods that are relatively symptom-free. However, many patients suffer from permanent symptoms with no remission periods.

Drugs that are used to treat the disease, including aminosalicylates, steroids, immunosuppressive drugs or biologicals such as Infliximab (an antibody against the tumour necrosis factor), are
designed to reduce the inflammation activity. Unfortunately, causal treatment is impossible since the genesis of the disease is unknown. Many patients are entirely dependent on permanent treatment with cortisone, despite the severe side effects associated with this hormone.

Defective mucosal barrier

The mucosa of the colon is covered with a tight layer of mucus which prevents the colon cells from coming into direct contact with stool and the bacteria contained therein. The mucosal barrier consists mainly of phosphatidylcholine (PC), a phosphorous-containing lipid better known as "lecithin". It forms a water impermeable protective layer, which is a prerequisite for protecting the mucosa directly below.

Prof. Dr. Wolfgang Stremmel, Medical Director of the Medical Clinic IV (Gastroenterology and Infectious Diseases) at the University of Heidelberg, and his team have found that ulcerative colitis is the result of a defective mucosal layer in which the PC content of the mucus is much reduced. The Heidelberg researchers were able to show that PC is actively secreted into the mucus, mainly in the posterior section of the small intestine, but hardly at all into the colon itself. The PC-containing mucus formed in the small intestine slowly but surely migrates through the colon towards the rectum. On its way to the rectum, the concentration of PC diminishes as it is degraded by the bacteria in stool, with the result that the lowest PC concentration is found in the rectum. That is where ulcerative colitis starts to develop.

Based on these findings, Prof. Stremmel and his team developed a new treatment concept: they were hoping to find a substitute for PC in order to strengthen the protective capacity of the colon and reduce inflammation. The simplest idea, i.e. the consumption of lecithin-rich food (e.g., bananas, chocolate, ice cream), seems to be a very attractive option for countering the disease, but unfortunately it does not lead to the desired effect. Lecithin consumed with food is degraded by the enzymes of the pancreas and is already completely absorbed in the small intestines, making it unable to reach the colon.

Slow release

For this reason, the researchers developed a special formulation, i.e. granules, which are only released in the lower part of the small intestine, from where they are able to coat the colon with PC and stabilise the defective protective barrier. This strategy was investigated in three clinical trials and led to impressive therapeutic results and either just a few or no side effects at all. In a first double-blind trial in 2005, the researchers found that patients suffering from permanent ulcerative colitis symptoms experienced a considerable improvement in their condition when they took the slow-release PC granules. The only noteworthy side effect experienced by the patients was flatulence, which resulted from the special packaging material used. A second trial showed that the
majority of patients suffering from permanent ulcerative colitis symptoms no longer required cortisone when they were given the PC granules. The disease did not become worse and a remission of the disease was observed in 50 per cent of the patients. In a third trial involving patients with ulcerative pancolitis, the researchers were able to determine the optimal dose of the slow-release PC granules. The next step involves the approval of the PC granules as a drug, which will allow all ulcerative colitis sufferers to have access to the drug. This step is being undertaken by the biotechnology company Lipid Therapeutics, established in early 2008 in Heidelberg with start-up financing from the EMBL Technology Fund.

Lipid Therapeutics

The objective of Lipid Therapeutics GmbH is to develop new therapies for the treatment of inflammatory diseases of the intestinal tract. At present, the company is focused on the clinical development of LT-02, a specific slow-release formulation of highly pure PC. Dr. Gerhard Keilhauer is the managing director of Lipid Therapeutics. The neurobiologist has extensive experience in the research and development of drugs in pharmaceutical and biotechnology companies. Prior to his present post, Keilhauer held senior positions at BASF BioResearch in Cambridge, Mass., USA and Knoll AG, Ludwigshafen, Germany and was also the Chief Development Officer at 4SC AG in Martinsried, Germany.

On 30th September 2009, Lipid Therapeutics announced the signing of a contract with Dr. Falk Pharma GmbH in Freiburg on the joint development of the company's lead product for the treatment of ulcerative colitis. Dr. Falk Pharma GmbH is a large pharmaceutical company specialising in diseases of the gastrointestinal tract and the liver. The two companies will test LT-02 in a large multicentre, European-wide clinical phase IIb trial. The companies have already received the go-ahead from the Ethics Commission in Heidelberg and from the German BfArM (German Federal Institute for Drugs and Medical Devices). Upon the successful conclusion of the trial, Dr. Falk Pharma will be able to carry out trials for obtaining European marketing authorisation for the drug. "We are very proud of the progress that we have made with LT-02 and its innovative principle of action," said Keilhauer adding: "We are very pleased to work with Dr. Falk Pharma, one of the leading European specialists in the field of chronic inflammatory intestinal diseases, whose primary goal is to offer patients new and effective treatment options."

Ulcerative colitis patients can now live in the hope that an effective drug will be available to them in the not too distant future.

Further information:

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