One focus of Immundiagnostik is laboratory diagnostics in gastroenterology. Our portfolio has continuously grown in the past years, fed by exclusive proprietary developments (ELISA, PCR) for routine and research in the areas of colon cancer detection, chronic inflammatory bowel diseases, exocrine pancreas diagnostics, food intolerances as well as infectious diseases. We have now expanded the latter area by complementing our product portfolio in the diagnostics of viral and bacterial infections with ELISA-products from Genzyme-Virotech. We are hence proud to offer our customers a comprehensive, automatable stool diagnostics programme featuring double controls for improved diagnostic accuracy, 1-point calibration ELISA-tests and stool sample tubes for hygienic handling.

**PCR analysis of spinal muscle atrophy**

Spinal muscle atrophy is caused by a defect in the spinal motoneuron gene (SMN). 95% of all affected patients have an altered or missing SMN1 gene as well as a reduced number of SMN2 gene copies.

→ **MutaGEL® SMN (KE 09021)**
Determination in whole blood

**NEW: PCR isolation of viral RNA from stool**

The MutaCLEAN® Stool (viral RNA) extraction kit purifies nucleotides (viral RNA, but also DNA) from the complex matrix stool in only a few minutes. The resulting high-quality RNA can be used for many applications of our RT-PCR virus diagnostic portfolio, e.g. for our Enterovirus or Influenza (A&B) real time PCRs. The extraction kit is of particular value for sample preparation in our successfully established Norovirus real time PCR kits (QCMD 2010-conform) - ideal for the now beginning „epidemic“ winter season.

→ **MutaCLEAN® Stool (viral RNA) (KG1034)**
Nucleotide extraction (RNA) from stool samples

**Malondialdehyde detection now in urine**

The quantitative determination of malondialdehyde (MDA) with HPLC is a meaningful parameter for lipid oxidation which is a risk factor for atherosclerosis. MDA analysis therefore is a significant tool in the diagnosis of oxidative stress. With our advanced HPLC kit it is now possible to determine MDA in urine.

→ **Malondialdehyde HPLC (KC 1900)**
Determination in plasma, serum, urine

**RBP-4 determination provides valuable information on vitamin A status**

The retinol binding protein 4 (RBP4) is responsible for the transport of vitamin A in circulation and therefore serves as a surrogate marker for the concentration of vitamin A (retinol) in serum. Our ELISA allows the quantitative determination of free RBP/RBP4 as well as RBP4 complexed with transthyretin. The assay is a practical alternative to the vitamin A analysis with HPLC and is therefore the ideal routine tool - now also available as 1-point calibration kit.

→ **RBP4 ELISA (K 6120)**
Determination in plasma, serum, urine

We gladly send you manuals and literature regarding our tests upon request

**LATEST NEWS ON VITAMIN B₆**

**Vitamin B₆ correlates with colon cancer**

Larsson et al. (2010):
"Vitamin B₆ and Risk of Colorectal Cancer". JAMA 303:11, 1077-1083

Vitamin B₆ acts as a coenzyme in numerous enzymatic reactions of the human metabolism. One of its major tasks is the transfer of one-carbon groups in DNA-synthesis and DNA-methylisation. Due to this pivotal role in the control of genetic information, Larsson and colleagues postulate in their actual publication (s. above) that a lack of vitamin B₆ is associated with a higher risk of colorectal cancer. This assumption is based on a large body of publications which confirms a protective role of the vitamin in the pathogenesis of colon cancer.

To test their hypothesis, the authors conducted a systematic meta-analysis of prospective clinical trials and explored the correlation of vitamin B₆ intake or blood levels of its active form pyridoxal 5’-phosphate (PLP) with the risk of colorectal cancer.

The results of this literature analysis indicate that elevated PLP blood levels are inversely associated with the risk of colon cancer: A rise of PLP-concentration of 100 pmol/ml cuts the risk almost in half. The correlation of vitamin B₆ intake and risk of colorectal cancer amounts to a 20% reduction in subjects with high intake.

These data imply that high vitamin B₆ or PLP blood levels exhibit some protection from colon cancer.

In addition to its HPLC-analysis kits, Immundiagnostik offers a cost-effective, practical alternative for the determination of biologically active vitamin B₆:

The ID-Vit® Vitamin B₆ microtiter plate test is a microbiological assay for the determination of total vitamin B₆ (PLP) in serum. The 96-well assay plate can be analyzed with a standard ELISA-reader.

**ID-Calprotectin ELISA superior to Bühlmann-ELISA in diagnostic accuracy**

Loitsch et al. (2010):
"Comparison of two commercially available serologic kits for the detection of fecal calprotectin". Gastroenterol 138:5, Suppl 1, S-528

The group of Prof. Dr. Dr. J. Stein at the University of Frankfurt introduced a Poster at this year’s DDW (digestive disease week) conference that compares the calprotectin ELISA from Immundiagnostik with that from Bühlmann (s. above citation).

The role of calprotectin as faecal inflammation marker draws a lot of attention. Thus, the comparison of publications and their data acquisition with commercial tests is of high interest. Here, the authors compared two human calprotectin ELISA-based assays commonly used in Europe (from Immundiagnostik and from Bühlmann) and tested them on 274 patients with acute diarrhea of unknown origin. Sensitivity, specificity and accuracy of the assays in the diagnosis of chronic inflammatory bowel diseases (IBD) and their activities as well as in the diagnosis of bacterial diarrhea were determined.

Both calprotectin tests provide a reliable and simple non-invasive means in the differentiation of inflammatory bowel disease and bacterial diarrhea from irritable bowel syndrome. However, the Immundiagnostik ELISA represents the most accurate marker (s. table).

<table>
<thead>
<tr>
<th>Test</th>
<th>Cont (n=96) vs active IBD (n=77)</th>
<th>Cont (n=96) vs active Colitis (n=36)</th>
<th>Cont (n=96) vs active CD (n=41)</th>
<th>IBD active (n=77) vs remission (n=31)</th>
<th>Cont (n=96) vs bacter. diarrhea (n=70)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calp-Bü</td>
<td>78.6%</td>
<td>75.3%</td>
<td>72.9%</td>
<td>80.6%</td>
<td>72.9%</td>
</tr>
<tr>
<td>Calp-ID</td>
<td>82.1%</td>
<td>85.2%</td>
<td>82.5%</td>
<td>81.5%</td>
<td>78.9%</td>
</tr>
</tbody>
</table>

Excerpt from table 1 (Calp-Bü = Bühlmann ELISA, Calp-ID = Immundiagnostik ELISA, Cont = Control)
Myostatin level linked to exercise-dependent insulin resistance

Myostatin belongs to the TGF-β (Transforming Growth Factor-β) super family and is known as a negative regulator of muscle growth. The protein is synthesized in muscle and released into the circulation where it binds locally or systemically to specific receptors. One of its major effects is the inhibition of proliferation and differentiation of myoblasts. A pharmacological or genetic blockade of the myostatin signal transduction pathway leads to a hypermuscular phenotype.

Hittel and co-authors found in previous studies that the myostatin level in muscle and plasma correlates with body weight and the severity of an insulin resistance. They concluded that therefore, myostatin plays a crucial role in the signalling cascades that regulate insulin sensitivity. In addition, they postulated that the myostatin concentration should change in response to insulin modifying actions such as physical exercise or weight loss.

To test this hypothesis, myostatin concentrations in muscle and plasma were determined in ten prediabetic, insulin resistant men before and after six months of moderate aerobic training. In addition, mice were injected with high concentrations of recombinant myostatin to investigate the causal relation between myostatin and the development of insulin resistance.

The quantitative myostatin analysis was performed with the EIA from Immundiagnostik. Myostatin protein levels were shown to decrease in muscle and matching plasma samples with aerobic exercise. Furthermore, the strong correlation between plasma myostatin levels and insulin sensitivity ($r^2 = 0.82$) suggested a cause-effect relationship that was subsequently confirmed by inducing insulin resistance in myostatin-injected mice.

**The study demonstrates that**

- Myostatin levels are regulated by aerobic exercise
- Myostatin is in the causal pathway of acquired insulin resistance with physical inactivity

Immundiagnostik offers a new, world-wide exclusive EIA for the quantitative determination of myostatin.

→ Myostatin (EIA) (K 1012)

*The Si is a degree to measure insulin dependent glucose uptake in tissue: 
$\text{Si} = \text{GIR mean} / \text{insulin concentration steady state}$. 
GIR mean is the constant glucose infusion within the last 45 min of the clamps. Insulin steady state is the constant insulin concentration during the steady state of the last 45 min of the clamps.*
EVENTS & ACTIVITIES

- **MEDICA**
  17. – 20. November 2010, Düsseldorf
  Booth Hall 3, E 59

- **Arab Health**
  24. – 27. January 2011, Dubai, United Arab Emirates
  Booth Nr. MG58

- **ECCO (European Crohn’s and Colitis Organisa- tion) Congress**

MEETING SUMMARIES

**ASBMR: Rising star myostatin**

Immundiagnostik had the traditional booth again at the American Society for Bone and Mineral Research (ASBMR) conference in Toronto, Canada. As usual, Vitamin D was at the centre of the delegates’ interest. This year for the first time, many inquiries were received about our unique Myostatin ELISA. The number of abstracts/presentations and discussions among delegates about this parameter has increased significantly. We expect this development to continue and intensify during the next years.

**UEGW: Strong international interest in comprehensive gastro-portfolio**

Immundiagnostik participated with a booth at the biggest and most important gastroenterology conference in Europe, the UEGW - this year in Barcelona. Our distributor in Spain, Laboratorios LETI, provided valuable support to our team by sending their product manager Raquel Mendez along. The attendance at the booth was quite vivid with a pronounced rise in visitors from Eastern European countries.

As at previous conferences, the delegates showed overwhelming appreciation for our Calprotectin ELISA and Rapid Test as reliable and convenient tools to diagnose and monitor bowel inflammation. Furthermore, our unique offer of tests systems to monitor Remicade® and Humira® drug levels and autoantibodies was seen as an exciting opportunity to ultimately arrive at the optimal individualized treatment for patients suffering from Crohn’s disease or Ulcerative Colitis.

Praxis to the **POINT**

**TIP:** Water quality critical for successful ELISA analysis

The accurate performance of immunoassays requires the use of ultrapure water. This high quality is achieved by exposing deionized water e. g. to reverse osmosis, ion exchange filtration, ultrafiltration or photo-oxidation so that its conductivity at 25°C is below 0,055 µS/cm (ISO 3696, grade 1). To ensure reproducible, error-free ELISA results, the ultrapure water should always be pyrogen-free and sterile filtered. As a matter of course the transport and filling of ultrapure water always occurs in contamination-free, pure laboratory vessels. Ultrapure water should not be stored since chemical components of the container or atmospheric CO₂ could impair the water quality.

MARKETING

Whenever a new parameter is sold for the first time by one of you, our distributors, we obviously are happy to learn the news. Well, firstly, this is a success for you and your sales team. At the same time we feel that it will be of high interest to learn why this particular customer has developed an interest in this particular parameter or kit, why they decided to purchase the kit, and which question in research or which service in routine they want to pursue.

Immundiagnostik would like to encourage all our partners in various countries to keep an eye on such first-time-purchases and try to find out the reasoning behind it. We are convinced that the obtained information will be helpful for all of us to enable and expand future sales. Thank you very much in advance.