Customer case study
Field of study: Gene Expression Profiling

Interpretation of gene expression data to tackle inflammatory bowel disease

Ingrid Arijs has a very personal connection to her research. As a patient with Crohn's disease, her investigations of inflammatory bowel disease (IBD) – which encompasses Crohn's and ulcerative colitis – are driven by a keen understanding of the impact these conditions have on people's lives.

In addition to her role as project manager of the collaboration between the medical and scientific activities within Jessa Hospital and the University of Hasselt in Belgium, Dr. Arijs is a postdoctoral scientist at the IBD KU Leuven research group in Belgium

and has spent the past decade working to unravel the biological complexity of these disorders. In recent studies, her efforts have yielded clinically important discoveries, such as finding a gene signature that appears to predict patient response to a particular therapy.

Dr. Arijs focuses on gene expression because of its sensitivity to underlying changes in the tissue biology, but after running microarrays or next-generation sequencing workflows, she and her team are left with large tables of expression data – with far too many genes to look up manually. She has tried several analysis tools to streamline the process, but the clearest and most comprehensive results came from QIAGEN's Ingenuity Pathway Analysis (IPA). Now, Dr. Arijs relies on this solution to make sense of her gene expression data and make new discoveries.

Exploring IBD

According to estimates, some 3.7 million people in the European Union alone have been diagnosed with IBD, primarily with Crohn's disease or ulcerative colitis. These conditions share many symptoms that affect quality of life – including chronic diarrhea, abdominal pain, bloody stools and more. IBD also contributes to increased risk of colon cancer, blood clots and bowel obstructions, among other health-threatening situations.

For her research, Dr. Arijs studies dysregulation of gene expression, comparing IBD patients to healthy controls or monitoring expression patterns in patients who respond well to therapy versus those who do not. Her team analyzes mRNA and microRNA from intestinal tissue collected during endoscopies. Once differentially expressed genes or miRNAs are identified, Arijs loads them into IPA to identify biological functions, networks and pathways that are most significant to the data sets of differentially expressed genes using the Downstream Effects Analysis tool and the Canonical Pathway tool. She also uses IPA to learn more about promising candidates, predict upstream transcriptional drivers and correlate miRNA and mRNA expression using the microRNA Target Filter. Finally, IPA shows Dr. Arijs the direct and indirect interactions between genes and allows her to draw and to visualize whole pathways in a network.

In a recent project, this approach led to the identification of a five-gene signature indicating likely response to a commonly used therapy for Crohn's patients. "This is a good way to identify a predictive signature or biomarkers for diagnosis or prognosis," Dr. Arijs says. When she first explored these five genes in IPA, she recalls, they immediately made sense: all were involved in immune-related pathways.

Another study was the first to focus on genome-wide alternative splicing in Crohn's disease patients. An analysis of samples retrieved from

19 patients and six healthy controls revealed 350 alternative splicing events spanning more than 240 genes. A deeper dive showed a distinct pattern in alternative splicing events for Crohn's patients compared to the controls. One of the genes involved, ICAM3, is found in a region previously known to confer susceptibility to the disease.

For Dr. Arijs, studying miRNA expression can be just as important as mRNA expression. In a recent project, she and her colleagues used both of these measures to determine the molecular profile of the early stages of Crohn's disease with the goal of identifying patients at a point when interventions have the highest chance of success. By integrating analysis of differential expression for both miRNA and mRNA, her team identified 64 miRNA-mRNA pairs with negative correlation in post-operative-recurrent patients. "IPA has a user-friendly tool where you can put in both mRNA and microRNA data sets and see whether there's a correlation," Dr. Arijs says. "It also flags interactions of mRNA and microRNA that have already been investigated, with links to the relevant literature."

The IPA advantage

At the start of her research career, Dr. Arijs tried other gene expression analysis tools, including several free options, but felt that IPA offered the best experience and results. Some tools were too basic, providing no opportunity for the deep biological dive that's possible with IPA. Others required too much bioinformatics expertise, forcing users to write and edit scripts for each analysis or making it very difficult to interpret results.

With its in-depth information and link to the extensive QIAGEN Knowledge Base for access to relevant peer-reviewed literature and other databases, IPA gives biologists like Dr. Arijs the ability to perform sophisticated analyses without needing a bioinformatics colleague for help. "You don't need to add statistical codes or scripts," Dr. Arijs says. "It's just click, click, click." She recommends that new users watch simple tutorial videos to get started quickly. "Everyone with a biomedical background can use IPA," she adds.

Perhaps most importantly, IPA dramatically reduces the amount of time Dr. Arijs would otherwise have to spend on analysis. From the manual approach – looking up genes individually in PubMed or NCBI – to programs that are harder to use and offer less information, most options involve a significant time commitment. "IPA saves me many hours," Dr. Arijs says, and it gets her moving more quickly to the next study.

"IPA has a user-friendly tool where you can put in both mRNA and microRNA data sets and see whether there's a correlation.

QIAGEN Bioinformatics

EMEA
Silkeborgvej 2 · Prismet
8000 Aarhus C
Denmark
Phone: +45 8082 0167
E-mail: bioinformaticssales@qiagen.com

Americas
1001 Marshall Street, Suite 200, Redwood City
CA 94063
USA
Phone: +1 650 381 5111 or **Toll Free:** +1 866 464 3684
E-mail: bioinformaticssales@qiagen.com