a reproducible model system, resulting in enteroctaneous fistulas
2–4w later. XGR samples were analysed by immunohistochemistry
staining (IHC) for EMT-, immune cell- and cell death markers.
Results: IHC staining of the XGR fistulas showed similar expression
patterns for various EMT markers (e.g. SNAIL1) like in human CD
fistula samples. The overexpression of the mesenchymal marker alpha-
smooth muscle actin confirmed the hypothesis that EMT plays a criti-
cal role for the fistula development in the XGR mouse model, too.
Moreover, collagen staining showed that the inflammatory regions
were associated with fibrosis suggesting extracellular matrix remodel-
ing. The inflammatory response up- and downstream to the XGR fis-
tula tracts mainly consisted of human CD45+ cells, but only very few
murine CD45+ cells. Further characterisation revealed CD4+ T cells
as predominant cell type in the fistulising samples. Also strong expres-
sion levels of human CD68+ cells were found in the XGR fistulas. The
overexpression of TNFα in the XGR fistulas samples emphasises the
importance of this mouse model, since this most likely represents a
novel platform for the evaluation of new therapies for fistulas in vivo.
Positive TUNEL and cleaved caspase-3 IHC staining in the XGR
fistula samples suggest apoptosis playing a role here, too.
Conclusions: Our data demonstrate that the in vivo model recap-
ituates both morphologically and mechanistically, human CD-associated fistulas. Establishing this novel in vivo platform,
could improve identifying unique treatment targets and help to eva-
uate new therapies.

P035
Serum markers predict outcome to ustekinumab
in patients with refractory Crohn’s disease and
provide insides in the mechanism of action
B. Verstockt1,2, S. Vermeire1,2, S. Verstockt3, C. Creyns4,
N. Ardeshir Davani2, C. Brennaert2, G. Van Assche1,2, G. Van
Assche1,2, M. Ferrante1,2
1University Hospitals Leuven, Department of Gastroenterology
and Hepatology, Leuven, Belgium, 2KU Leuven, Translational
Research in Gastrointestinal Disorders, Department of Chronic
Diseases, Metabolism and Ageing, Leuven, Belgium, 3KU Leuven,
Laboratory of Complex Genetics, Department of Human Genetics,
Leuven, Belgium, 4KU Leuven, Laboratory for Clinical Immunology,
Department of Microbiology and Immunology, Leuven, Belgium

Background: Ustekinumab (UST), targeting the IL-12/23 shared p40
subunit, was recently approved by FDA and EMA for treatment of
moderate-to-severe Crohn’s disease (CD). The aim of this study was
to identify potential predictive immunological biomarkers for
response, which may guide treatment strategies with ustekinumab.
Methods: Serum samples of 36 CD patients (73% female, median
disease duration 15.9 years), all refractory to anti-TNF therapy and
vedolizumab and with baseline endoscopic active disease, were pro-
spectively collected prior to UST initiation. Patients received UST
6 mg/kg IV at induction, with subcutaneous UST 90 mg q8w there-
after. Endoscopic response was assessed at week 24, and defined as
≥ 50% SES-CD decrease. Proteomic analysis (OLINK) was performed
on baseline serum samples. Additionally, inflamed ileal (n = 10) and
colic (n = 17) biopsies, prior to UST therapy, were collected. Mucosal
total RNA was isolated, and next-generation sequencing performed.
Differentially gene expression was evaluated by DESeq R package.
Results: Patients with (n = 7) and without (n = 29) endoscopic response
at week 24 had a similar baseline inflammatory burden, reflected by
similar median faecal calprotectin (1800 vs. 1721 μg/g, p = 0.22),
C-reactive protein (20.3 vs. 9.4 mg/l, p = 0.36) and IL-6 (p = 0.37, fold
change (FC)=1.06) before start of UST. Baseline endoscopic activity
was much higher in patients responding to UST, compared with non-
responders (median SES-CD 21 vs. 13, p < 0.001). Several proteins sig-
ificantly correlated with baseline SES-CD, but only one protein, CD40
(r = 0.87, p = 0.05), also significantly differed between responders and
non-responders before UST initiation (p = 0.029 with corresponding
FC 1.46). At baseline, CCL11 also varied between responders and non-
responders (r = 0.06, FC 1.45), but did not correlate with baseline
SES-CD (p = 0.97). ROC-statistics showed a significant area under the
curve (81.5%, p = 0.011) for prediction of response based on the com-
bination of both. On mucosal level, a non-significant increase in both
CD40 and CD40L could be observed in colonic biopsies of responders
at baseline (FC 1.6 and 1.5, respectively). Ileal biopsies also expressed
increased CD40L in responders (FC 2.0).
Conclusions: Two potential predictive biomarkers for response to
UST were identified, which need validation in larger and independ-
ent cohorts. Because it has been shown that CD40/CD40L-triggering
of dendritic cells induces expression of high levels of IL-23 and not
IL-12, low CD40 levels in non-responders suggest another mecha-
nism, apart from the IL-12/23 pathway, driving inflammation in
these patients. These findings may aid in individualised selection of
biological agents in Crohn’s disease, and provide mechanisms of pri-
mary (non-)response to UST.

P036
Faecalibacterium prausnitzii produces
butyrate to maintain Th17/Treg balance and to
ameliorate colorectal colitis by inhibiting histone
diacetylase 1
L. Zhou1, M. Zhang1,2, Y. Wang1, T. Yu1, X. Chen1, D. Tang1,
L. Xu1, Y. Yin1, Y. Pan1, Q. Zhou1, Y. Zhou1, C. Yu1,2
1Drum Tower Hospital, Medical School of Nanjing University,
Nanjing, China, 2Jiangsu Clinical Medical Center of Digestive
Disease, Nanjing, China, 3Fudan University, Nanjing, China,
4Zhongda Hospital, Nanjing, China, 5Huashan Hospital, Shanghai,
China, 6Fudan University, Shanghai, China

Background: Inflammatory bowel disease (IBD)-associated dysbiosis
is characterised by a loss of Faecalibacterium prausnitzii, whose
superantigen exerts an anti-inflammatory effect. However, the anti-inflam-
matory substances in F. prausnitzii supernatant are yet to be fully investigated.
Methods: Experimental colitis models were induced and evaluated
by clinical examination and histopathology. Levels of cytokines and
ratio of T cells were detected by enzyme-linked immunosorb-
ent assay and flow cytometry analysis, respectively. F. prausnitzii
supernatant was separated by microporous resin. After extraction,
the substances in supernatant were identified by gas chromatogra-
phy–mass spectrometer. T cell differentiation assay was conducted in
vitro. Changes in signalling pathways were examined by western
blot, immunohistochemistry and immunofluorescent staining.
Results: We found that the supernatant of F. prausnitzii could regu-
late T helper 17 cells (Th17)/ regulatory T cells (Treg) differen-
tiation. Then, we identified that butyrate produced by F. prausnitzii
that played the anti-inflammatory effects by inhibiting interleukin (IL)-6/
signal transducer and activator of transcription three (STAT3)/IL-17
pathway and promoting forkhead box protein P3 (Foxp3). Finally,
we demonstrated the target of butyrate was histone deacetylase 1
(HDAC1).