Abstract IDDF2019-ABS-0209 Table 2 Analysis results: 28 tissue-common pathways enriched in six tissues.

NAME	DATABASE
Activation of NF-kappaB in B cells;	reactome
Oxygen-dependent proline hydroxylation of Hypoxia-inducible Factor Alpha;	reactome
ER-Phagosome pathway;	reactome
Cross-presentation of soluble exogenous antigens (endosomes);	reactome
Autodegradation of Cdh1 by Cdh1:APC/C;	reactome
APC/C:Cdc20 mediated degradation of Securin;	reactome
APC/C:Cdh1 mediated degradation of Cdc20 and other APC/C:Cdh1 targeted proteins in late mitosis/early G1;	reactome
Cdc20:Phospho-APC/C mediated degradation of Cyclin A;	reactome
Vpu mediated degradation of CD4;	reactome
SCF(Skp2)-mediated degradation of p27/p21;	reactome
Formation of the beta-catenin:TCFtransactivating complex;	reactome
Downstream TCR signaling;	reactome
DNA Damage/Telomere Stress Induced Senescence;	reactome
FCERI mediated NF-kB activation;	reactome
Regulation of ornithine decarboxylase (ODC);	reactome
AUF1 (hnRNP D0) binds and destabilizes mRNA;	reactome
Asymmetric localization of PCP proteins;	reactome
Degradation of DVL;	reactome
Defective CFTR causes cystic fibrosis;	reactome
Retrograde transport at the Trans-Golgi-Network;	reactome
CDK-mediated phosphorylation and removal of Cdc6;	reactome
Ubiquitin-dependent degradation of Cyclin D1;	reactome
G2/M Checkpoints;	reactome
The role of GTSE1 in G2/M progression after G2 checkpoint;	reactome
FBXL7 down-regulates AURKA during mitotic entry and in early mitosis;	reactome
Regulation of PTEN stability and activity;	reactome
TGF beta receptor I degradation signaling (TGF-beta_super_family_signaling_pathway(canonical))	inh
Integrin signaling pathway (Integrin signaling pathway)	inh

Conclusions Totally, we proposed a new viewpoint as pan-tissue analysis and implemented a pathway-based computational approach to detect the critical difference and common pathways in the responsive tissues during T2D progression, and also shown that the tissue-common pathways can especially serve as genetic warning signals for the T2D sub-states (e.g.complications).

IDDF2019-ABS-0224 SECRETOME MODULATION OF CACO2 CELL LINE INDUCED BY A MULTI-STRAIN PROBIOTIC

¹Valentina Petito*, ²Viviana Greco, ³Lucrezia Laterza, ³Cristina Graziani, ⁴Stefano Colombo, ³Loris Lopetuso, ³Franco Scaldaferrì, ²Andrea Urbani, ³Antonio Gasbarrini. ¹Institute of Medical Pathology, Università cattolica del Sacro Cuore, Rome, Italy; ²Institute of Biochemistry and Clinical Biochemistry, Università cattolica del Sacro Cuore, Rome, Italy; ³Gastroenterological Area, Gastroenterological, Endocrino-Metabolical AND Nefro-urological Sciences Department, Fondazione Policlinico Universitario Gemelli IRCCS, Rome, Italy; ⁴Beingpharma S.r.l, Milan, Italy

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Background Probiotics are defined as live, non-pathogenic bacteria that confer health benefits beyond their nutritional value. Particularly VSL#3, a probiotic mix containing 4 strains of Lactobacilli (*L. paracasei*, *L. plantarum*, *L. acidophilus* and *L. delbrueckii* subsp. *bulgaricus*), 3 strains of Bifidobacteria (*B. longum*, *B. infantis*, *B. breve*) and *Streptococcus thermophilus*, has demonstrated efficacy in the management of diseases characterized by increased intestinal permeability. The aim of the present study was to study secreted bioactive factors in order

to evaluate the mechanisms of action to enhance intestinal epithelia.

Methods Two different lots of VSL#3 (Manufacturer: Nutrilinea Srl, Gallarate (VA) - Italy, lot #802097 and lot #802100) were used. Caco2 cell line were treated with a conditioning media (CM) prepared using 1g of probiotic formula grown in D-MEM cell culture medium (free of serum and antibiotics) at 37°C for 48 hours without shaking and in anaerobic conditions. Caco2 were treated with diluted CM at 1:10 and 1:25 for 24 and 48 hours. Media culture for each condition has been collected and analyzed by a deeper proteomics approach. Differential protein expression was evaluated by shotgun proteomics analysis based on nLC-HDMS^E and carried out on Synapt G2-Si mass spectrometer.

Results The analysis of supernatants from Caco2, treated with CM, showed the presence of bacteria strain-specific proteins. Human proteins synthesized from CaCo2 were also identified, such as caspase 1, IL8, HSP70, HSP70b, HSP90, HSP105. The productions were time- and dose-dependent. In CM diluted 1:10, probiotic-derived proteins have been shown to be more expressed at 24 hours. Human caspase 1, IL8, HSP 70, HSP 70b, HSP 90, HSP 105 were also found upregulated in Caco2 treated for 24 hours with CM diluted 1:10.

Conclusions This is the first time where a probiotic secretome was explored. Analysis of secretome from Caco2 treated with CM helped us to understand the mechanism by probiotics can enhance intestinal barrier: by strengthen the autophagy process, an arm of innate immunity, by overexpression of caspase 1, IL8 and HSP 70, and by HSPs dependent modulation of inflammation.