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► **To cite this version:**

Charles Le Bras, Nolwenn Jacquet, Lucie Rault, Nathalie Daniel, Victoria Chuat, et al.. Immunomodulatory impact of bacteria isolated from human breast milk. In vitro analysis. 8èmes Rencontres NAM2S Nutrition – Alimentation – Métabolisme – Sport – Santé, Biotech Santé Bretagne, Nov 2022, Rennes, France. hal-03881887

HAL Id: hal-03881887

<https://hal.inrae.fr/hal-03881887>

Submitted on 2 Dec 2022

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Immunomodulatory impact of bacteria isolated from human breast milk. In vitro analysis.

Charles Le Bras^{1,2}, Nolwenn Jacquet¹, Lucie Rault¹, Nathalie Daniel¹, Victoria Chuat¹, Florence Valence¹, Latifa Bousarghin², Amandine Bellanger³, Isabelle Le Huërou-Luron², Sergine Even¹

¹INRAE, Agrocampus Ouest, STLO, Rennes, France; ²INRAE, INSERM, Univ. Rennes 1, NUMECAN, Saint-Gilles, Rennes, France; ³CHU de Rennes, Département de Pédiatrie, Rennes, France

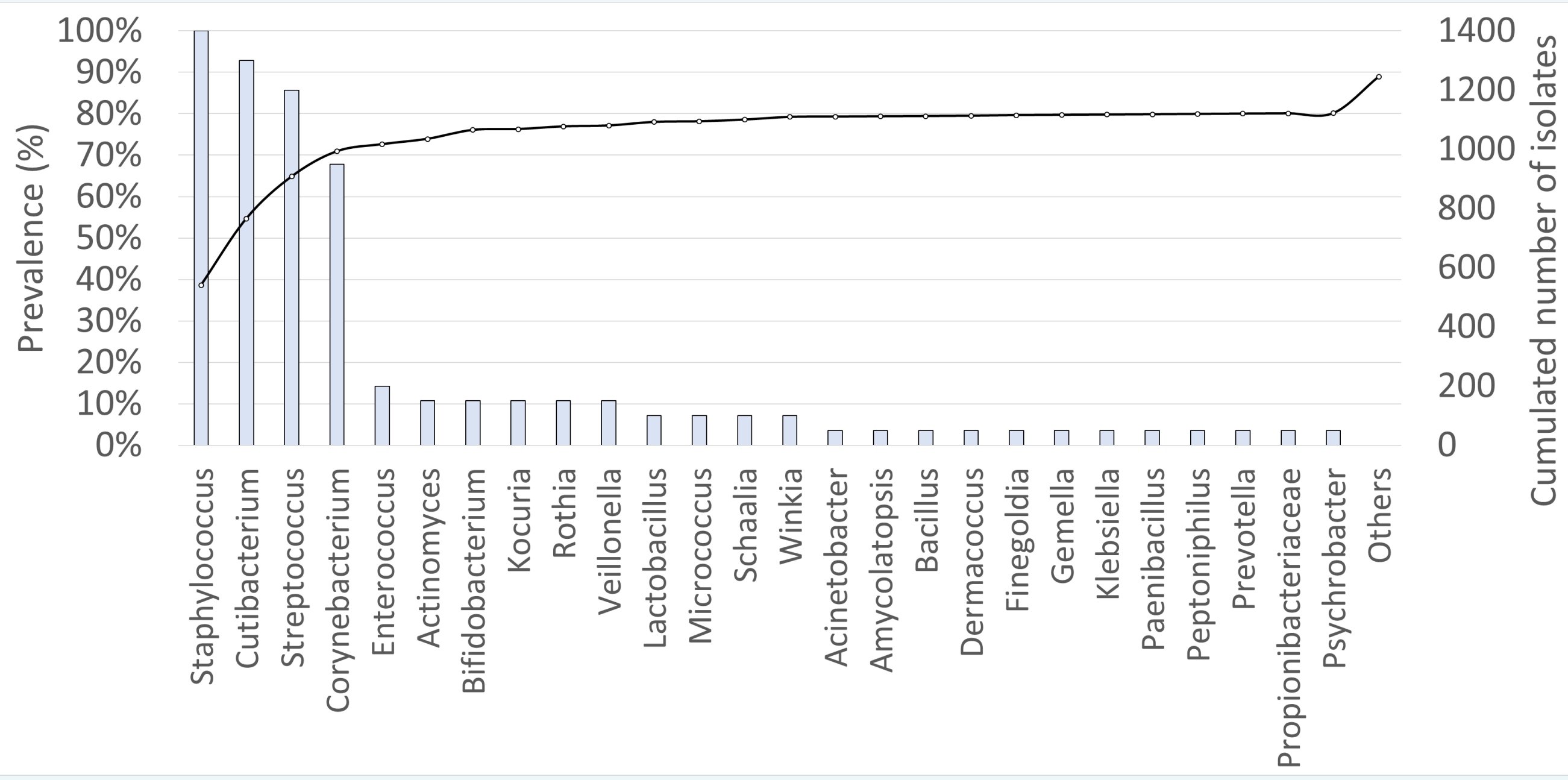
CONTEXT

Breastfeeding is recommended by the WHO for the first 6 months of life. Compared to infant formula (IF), human milk (HM) provides health benefits, including protection against intestinal and respiratory infections in early childhood and a lower risk of metabolic and immune diseases later in life. Discrepancies in health benefits are probably due to different nutritional and non-nutritional composition between IF and HM, the latter being more complex and richer in bioactive components.

AIM & STRATEGY

Our hypothesis is that HM health benefits come in part from the bacteria of the HM microbiota, which may promote the maturation of the immune system through their role on gut immune homeostasis. This study aimed to better understand the immunomodulatory role of HM bacteria. Bacteria were isolated from healthy breast milk and screened for their immunomodulatory potential on two different cellular models: PBMC (blood mononuclear cell) from 2 healthy donors and a multicellular model of intestinal epithelium enterocytes (Caco2), calciform cells (HT 29-MTX), M cells (differentiated Caco2) and macrophages (THP-1).

HM Bacteria collection



RESULTS

Figure 1: Human Milk bacteria isolated from 28 healthy donors during the first month of lactation. Prevalence of genera is indicated as well as the cumulated number of isolates.

- Diversity of the HM microbiota: 1245 isolates obtained, belonging to 26 genera and 56 species.
- These isolates include the **4 most prevalent taxa** associated to the HM (*Staphylococcus*, *Cutibacterium*, *Streptococcus* and *Corynebacterium*) and **22 genera** with lower abundance and prevalence, representative of the diversity of HM microbiota.
- 88 isolates were selected based on their prevalence and on representation of bacterial diversity in HM microbiota for further screening.

PBMC model

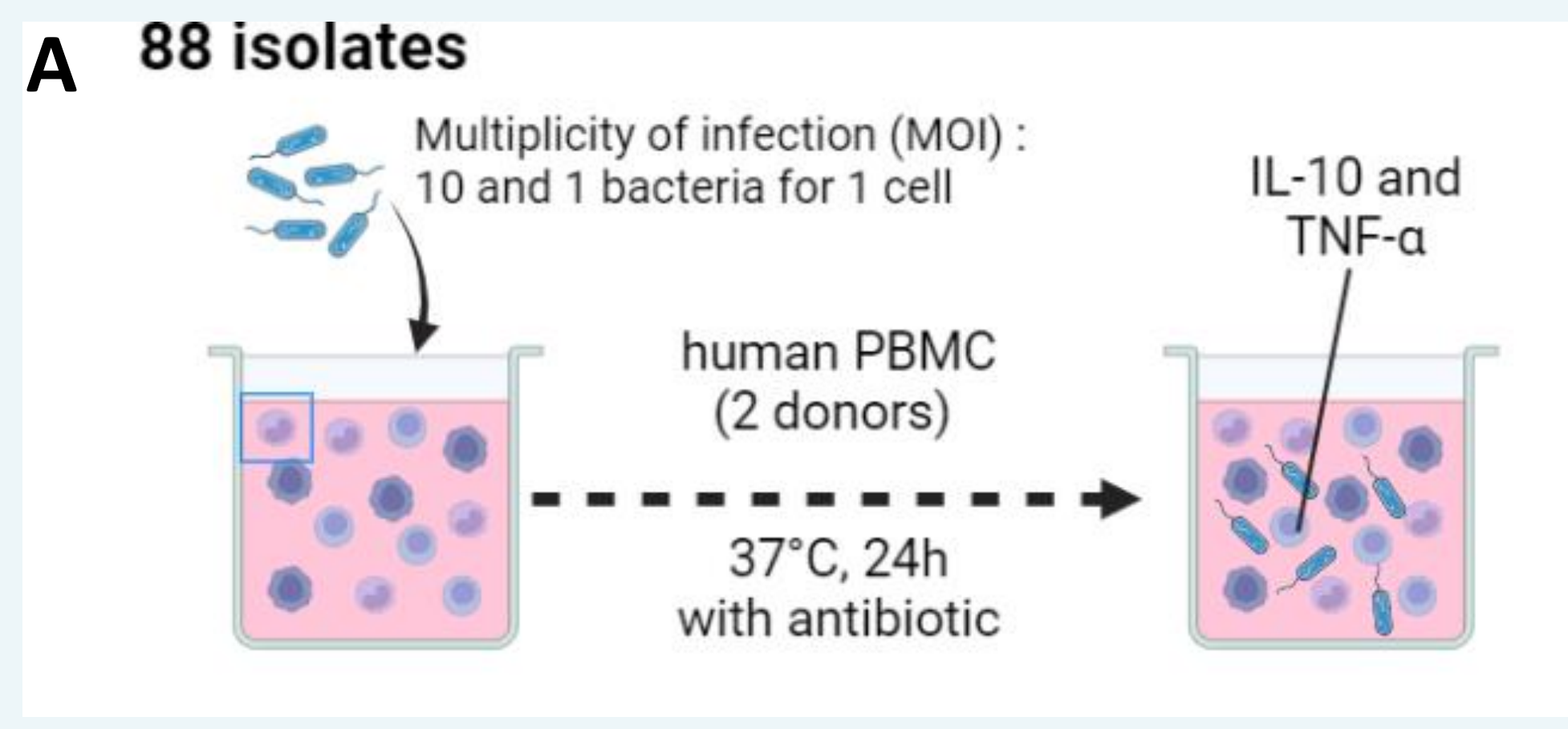
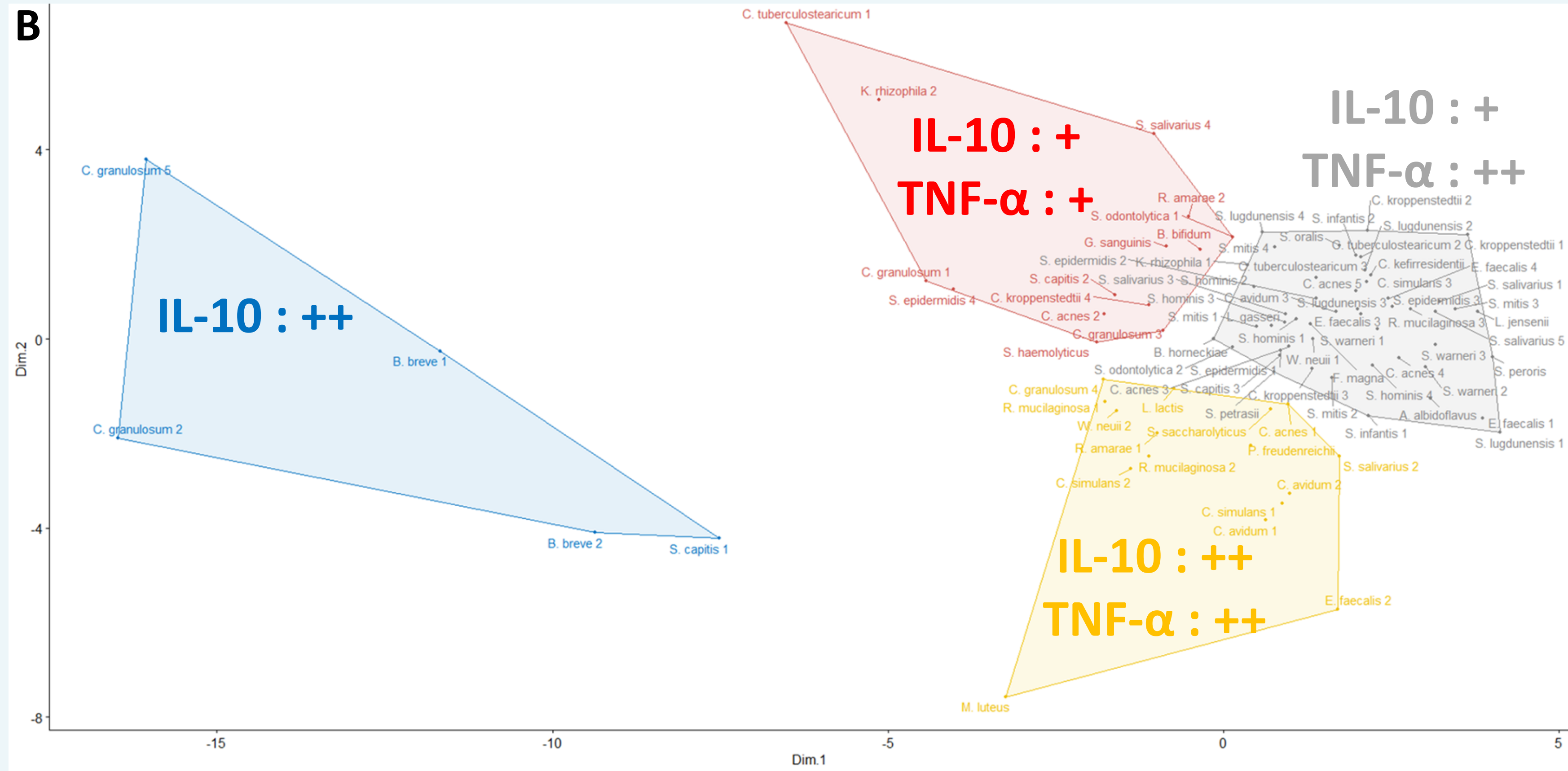


Figure 2: A. PBMC stimulation by HM bacteria; B. HM bacteria clustering by Multidimensionate scaling (MDS) with k-means clustering according to the production of IL-10 and TNF-α by PBMC stimulated by these isolates.



- The immunomodulatory effect was species- and strain-dependent.
- The 88 isolates were clustered into **4 groups**: anti-inflammatory, strong immunomodulatory, medium immunomodulatory and pro-inflammatory tendency.
- Some strains belonging to genera not described as probiotics (like *Staphylococcus*) exhibited anti-inflammatory potential.
- 28 isolates were selected based on their immunomodulatory properties.

Quadracellular model of intestinal epithelium

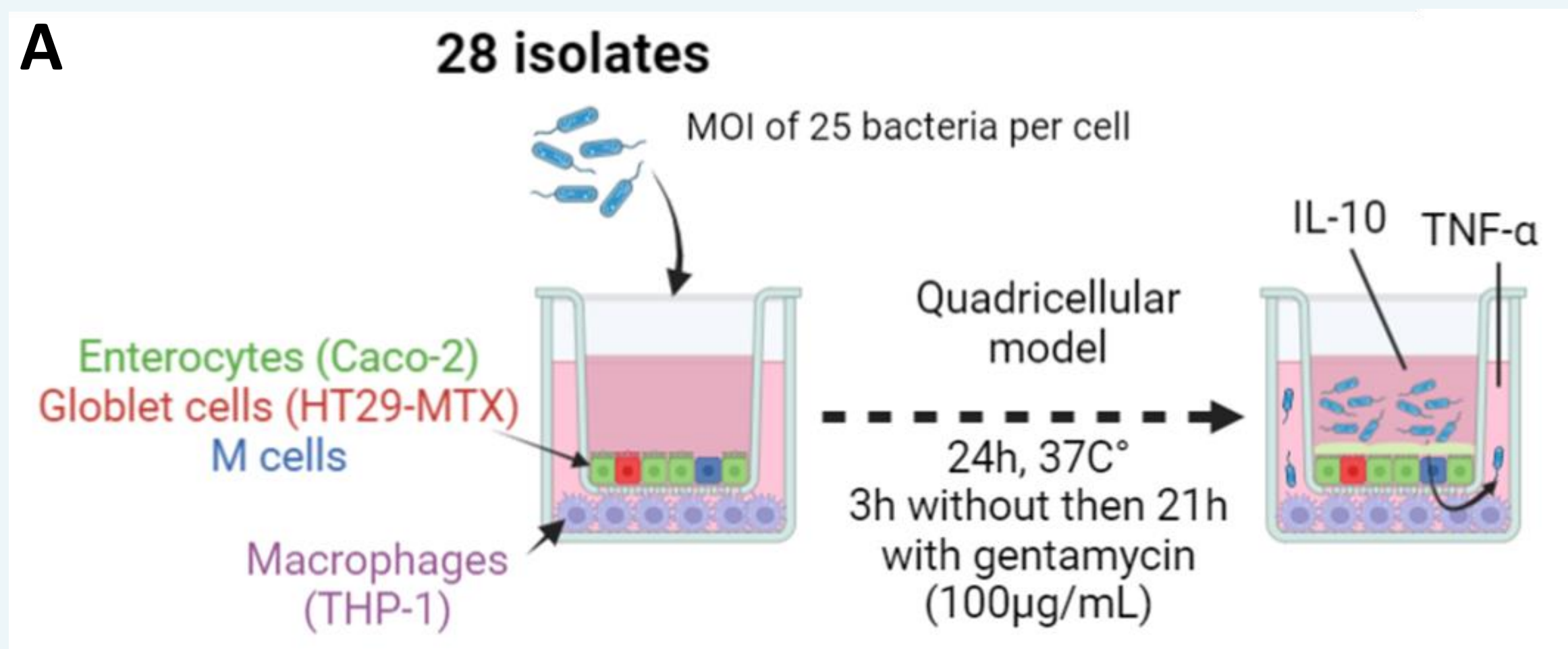
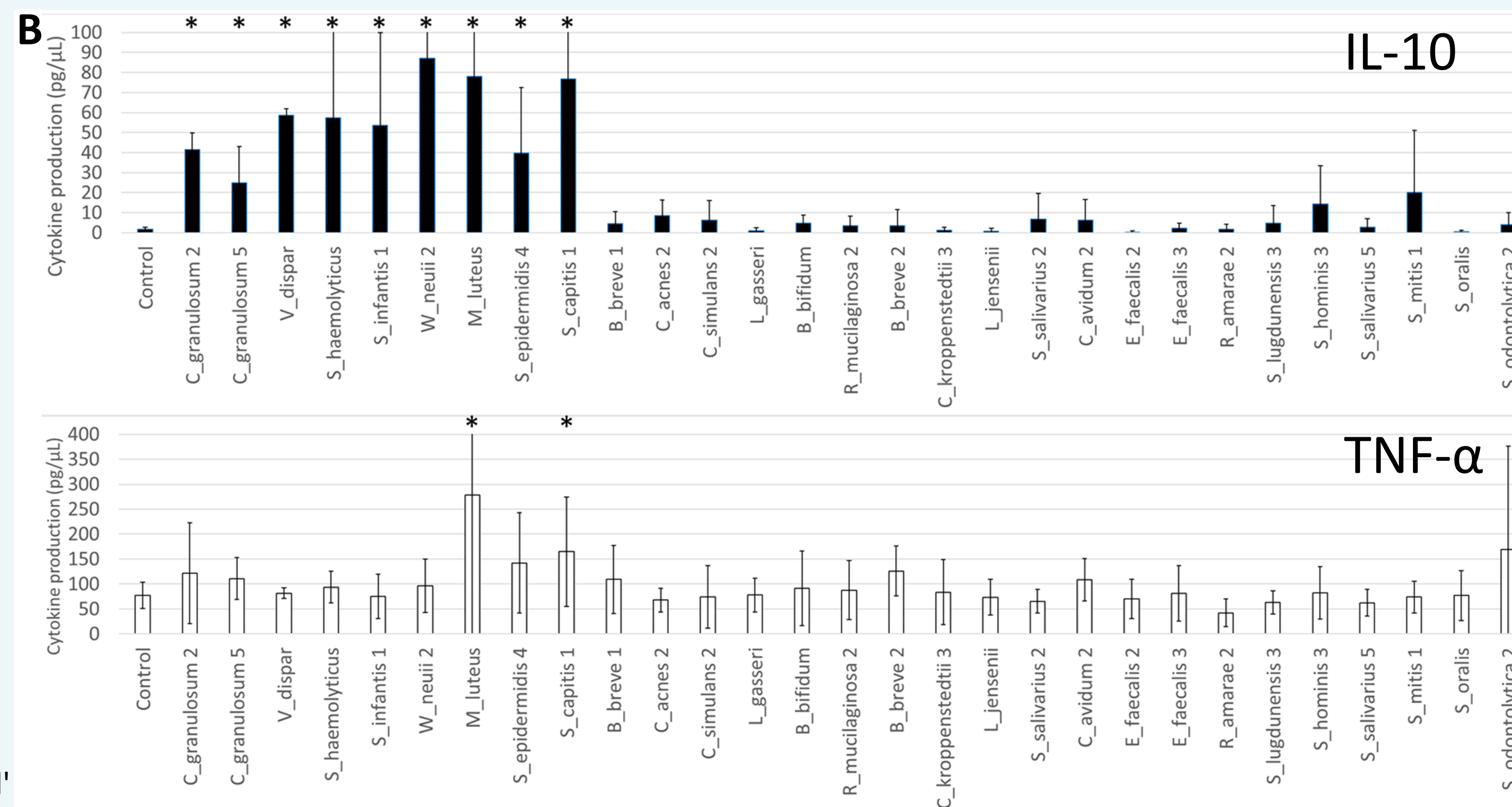


Figure 3 : A. Stimulation of the quadracellular model of intestinal epithelium by HM bacteria; B. IL-10 production (pg/mL) in the apical compartment and TNF-α production (pg/mL) in the basal compartment by the quadracellular model cells stimulated by each isolate.



* : P < 0.05 in comparison with 'control'

Isolates can be divided into **3 groups** based on IL-10 and TNF-α production: **dominant anti-inflammatory activity**, **immunomodulatory activity (both pro- and anti-inflammatory)**, **low or no immunomodulatory activity**.

CONCLUSION & PERSPECTIVES

Human milk bacteria have a significant immunomodulatory potential depending on species and strains, illustrating the potential of the HM bacterial community and the subtle balance between pro- and anti-inflammatory profile. Further investigations on the synergistic potential of these bacteria combined in consortia with different profiles (anti-inflammatory and strong immunomodulatory profiles) are in progress before characterising the impact of these bacteria in vivo (Yucatan mini-pig piglet model).