# Genomics of *Streptococcus macedonicus* : moving from pathogenicity to adaptation to the dairy environment


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## Abstract

**Background:**
**Lactic acid bacteria (LAB) constitute a significant group of microorganisms found in foods, but also contribute to human health. The *Streptococcus bovis/ Streptococcus equinus* complex within LAB includes members that have been implicated in human diseases, like endocarditis and colon cancer.**
**Objectives:**
**In this study we compared the three available genome sequences of *Streptococcus macedonicus* strains isolated from dairy products. Only one strain has its genome complete sequenced and previous analysis showed diminished pathogenic potential and adaptation to the milk environment. Here we present the *in silico* analysis of these strains, in order to better understand the *S. macedonicus* species.**
**Methods:**
**Chromosomal maps were constructed using DNAPlotter and whole genome sequence alignments were performed by progressiveMAUVE and Webact in order to visualize conserved genomic regions or chromosomal rearrangements. Genomic islands were identified and visualized by IslandViewer, potential bacteriocins were predicted by BAGEL3 and CRISPRs were analyzed by the tools available in the CRISPRcompar web-service.**
**Conclusions:**
**The analysis revealed that the strains have lost genes involved in the catabolism of complex plant carbohydrates, in the adhesion to the host's cells and in haemolysis. On the other hand, an extra lactose operon and a proteolytic system characteristic of LAB were identified. Even though our whole genome analysis of *S. macedonicus* shows adaptation traits to the nutrient-rich dairy environment, analysis of additional *S. macedonicus* genomes, including non-dairy isolates, may be necessary to clarify its pathogenic potential.**


## Results and Discussion

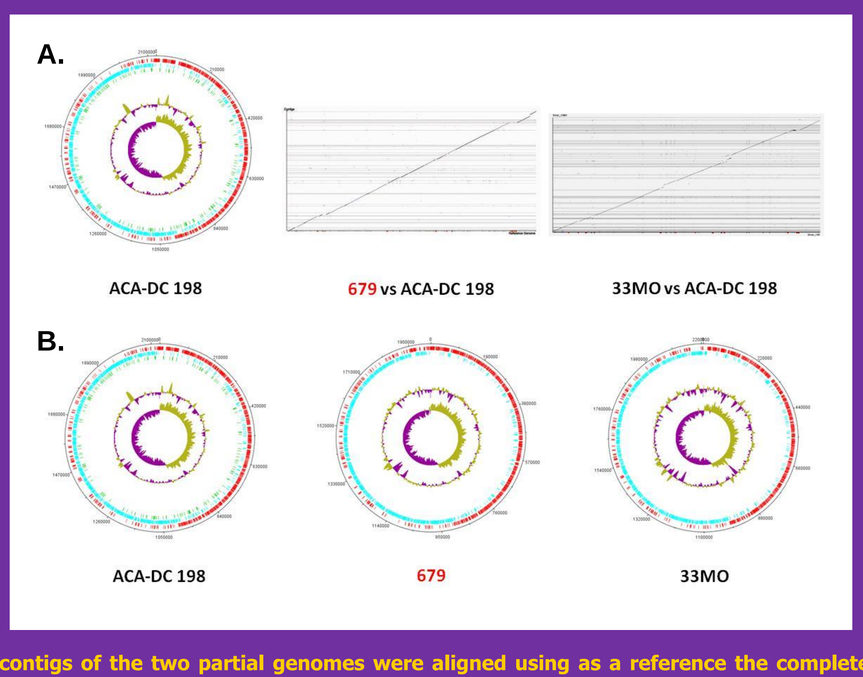



**Figure 1 – A. The contigs of the two partial genomes were aligned using as a reference the complete genome of the *S. macedonicus* ACA-DC 198 strain. B. Based on the alignments, the pseudochromosomes and the relevant maps were constructed.**

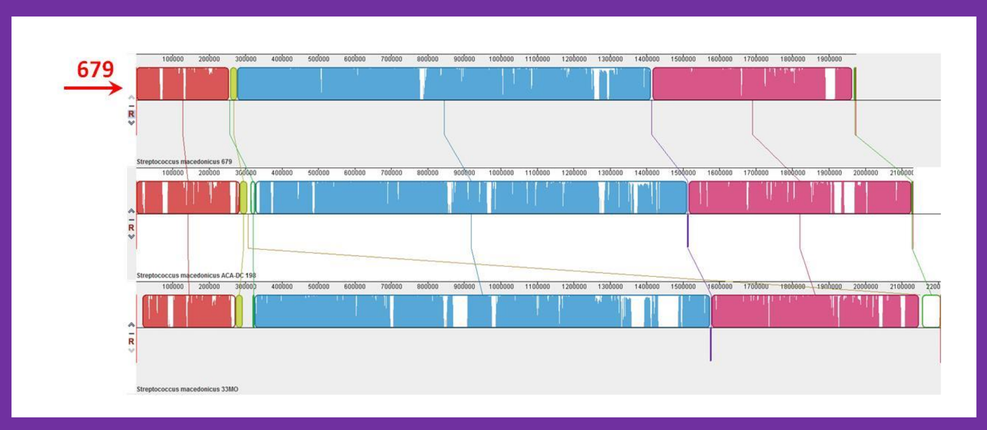



**Figure 2 – Chromosome alignments of the *S. macedonicus* strains were calculated by progressiveMauve. The local collinear blocks (LCBs) of conserved sequences among the strains are represented by rectangles of the same colour. Connecting lines can be used to visualize synteny or rearrangement. LCBs positioned above or under the chromosome (black line) correspond to the forward and reverse orientation, respectively. The level of conservation is equivalent to the level of vertical colour filling within the LCBs (e.g. white regions are strain-specific). Sequences not placed within an LCB are unique for the particular strain.**

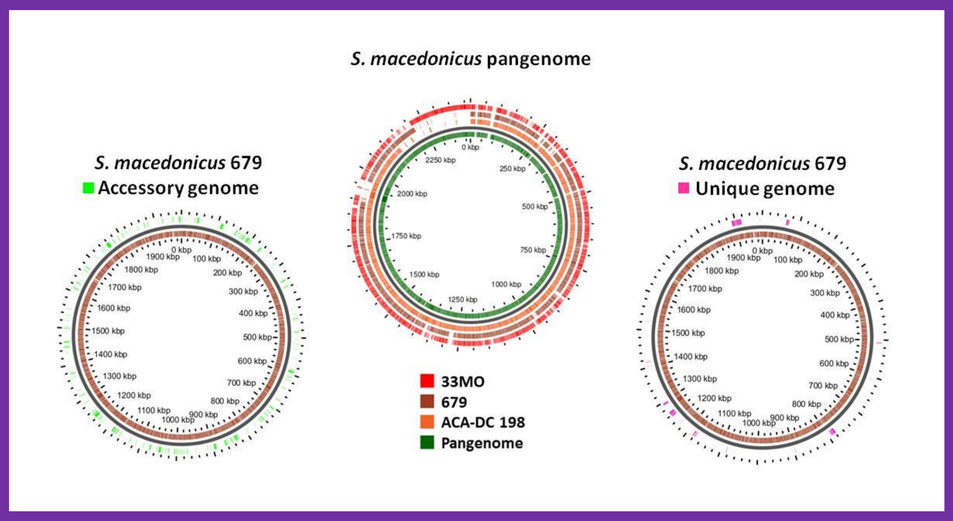



**Figure 3 – Further analysis showed that the pangenome of the *S. macedonicus* strains is comprised of approximately 2400 genes. Concerning the genome of 679 strain, a great number of genes were distributed among the core and the accessory genome, while the unique genome contained 250 genes.**

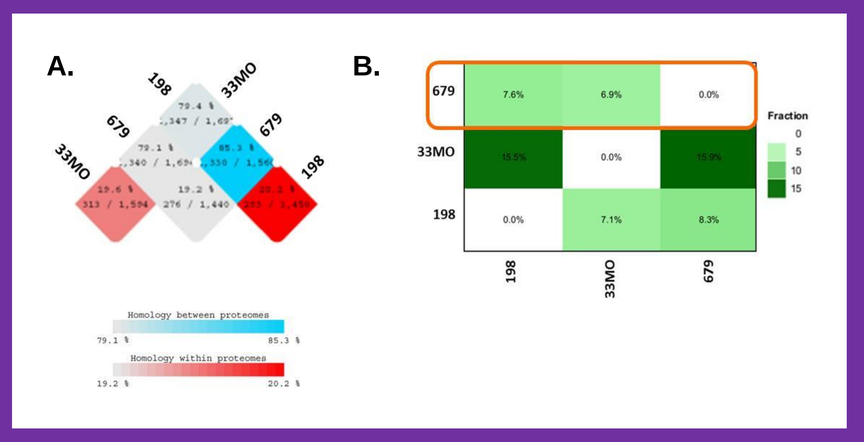



**Figure 4 – A. Pairwise pan and core comparison between the three *S. macedonicus* strains, showed that the pairs share 80-85% of the protein families. Homology estimation within the proteome, revealed that approximately 19% of protein families in the proteome of the 679 strain has more than one member. B. Proteomes were also compared in pairs to estimate the fraction of specific proteins which are present in one genome and absent in another. The proteome of the 679 strain has 7% specific proteins.**

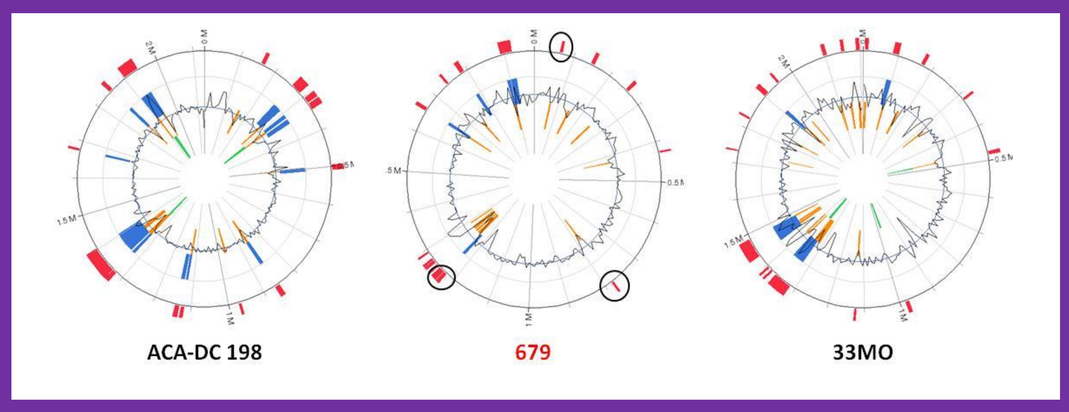
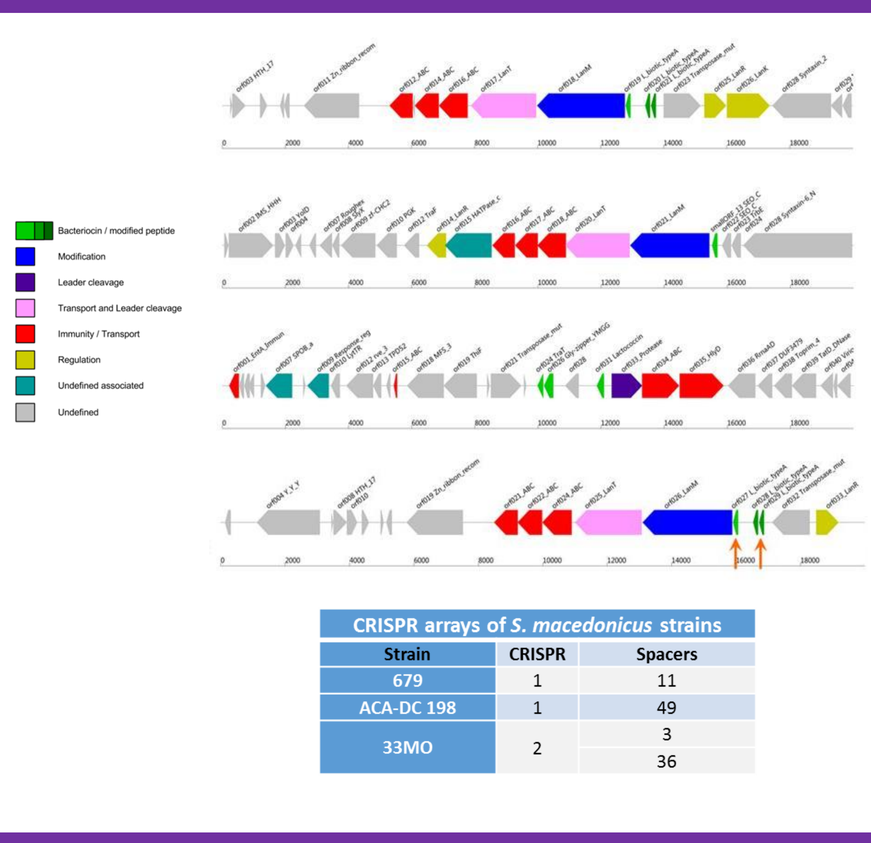



**Figure 5 – A great number of genomic islands in the three *S. macedonicus* strains were found. Specifically for the 679 strain we identified 5 unique genomic island, as indicated by the black circles.**




**CRISPR arrays of *S. macedonicus* strains**

| Strain | CRISPR | Spacers |
|---|---|---|
| 679 | 1 | 11 |
| ACA-DC 198 | 1 | 49 |
| 33MO | 2 | 3 |
| | | 36 |

**Figure 6 – A potential lantibiotic was predicted and BLAST analysis of the entire gene cluster showed high identity to the known bacteriocin macedocin of the ACA-DC 198 strain. The CRISPR analysis revealed the existence of 1 CRISPR and low number of spacers**


## Bibliography

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## Acknowledgments

**This work was financially supported by the THALES Program (Funded by the Greek General Secretariat for Research and Technology).**


FEMS 6th Congress of European Microbiologists 7 - 11 June 2015 Maastricht, The Netherlands

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NSRF 2007-2013 programme for development