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Carbon metabolism in *Streptococcus thermophilus*: co-utilization in mixtures and role of sugar nature and concentration in gene regulation

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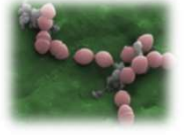
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Carbon metabolism in *Streptococcus thermophilus*: co-utilization in mixtures and role of sugar nature and concentration in gene regulation



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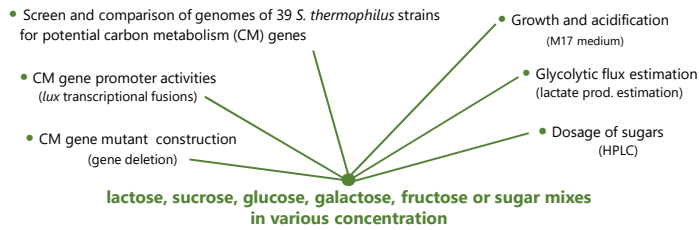
Context

Streptococcus thermophilus is a bacterium widely used in the production of yogurts and cheeses, where it efficiently ferments lactose, the saccharide naturally present in milk. However, when used in sweetened dairy products or plant-based products, *S. thermophilus* may encounter other saccharides (i.e. alone or in mixtures). To date, *S. thermophilus* growth and metabolic capacities in such contexts as well as carbon metabolism regulation mechanisms remain poorly characterized.

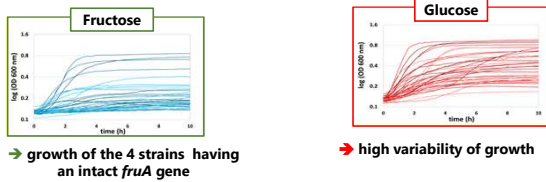
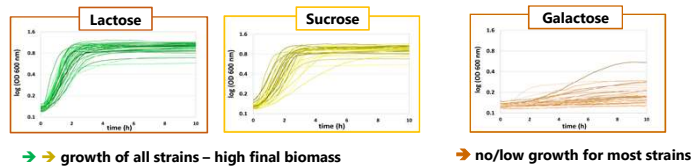
Questions

- Is there genetic and/or phenotypic diversity of sugar use in *S. thermophilus*?
 - What are the sugars consumed?
 - How is sugar metabolism regulated?
- in presence of single or mix sugars

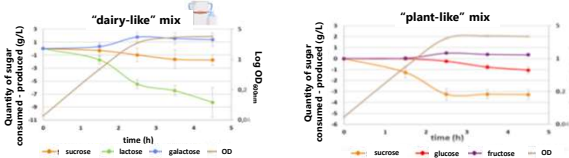
Methods



Bacterial growth, sugar consumption and glycolytic flux

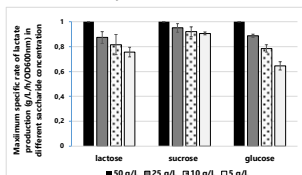


- S. thermophilus* LMD-9 first consumes
 - lactose over sucrose
 - sucrose over glucose
 when sugars are mixed



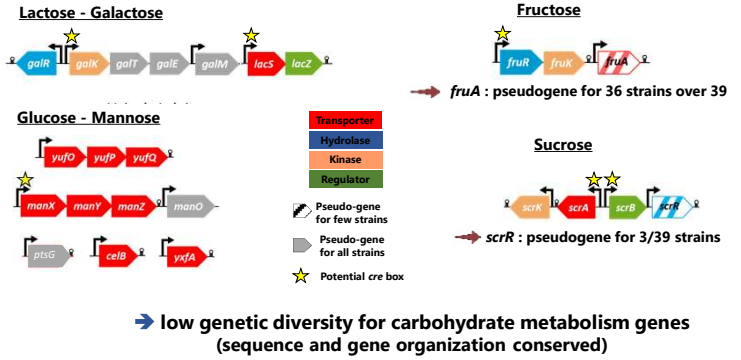
Lactate production

- is higher in presence of lactose or glucose, compared to sucrose
- decreases as lactose or glucose concentration decrease
- is not affected by sucrose concentration



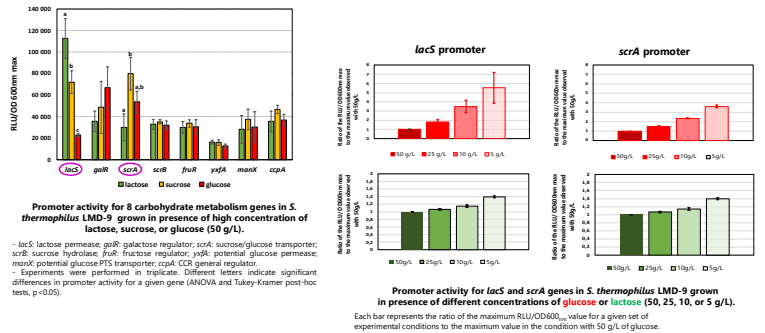
In silico analysis

- The 39 strains possess genes coding for the potential use of 5-6 carbohydrates



Regulation of carbon metabolism genes

- All promoters of CM genes tested are active in presence of lactose, glucose or sucrose and the activities of only lacS and scrA ones are modulated by the nature of the sugar



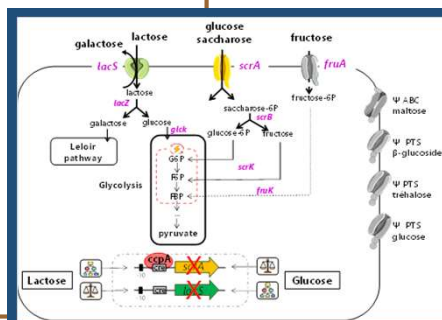
- Glucose and lactose repress promoter activity for transporter-encoding genes lacS and scrA in a concentration-dependent manner, whereas sucrose not

- Glucose maintains its repressive effects in mixed-saccharide media on lacS and scrA promoter activities



- lacS promoter activity is no more repressed in a ΔcpaA mutant, whatever the lactose or glucose concentration (10, 25 or 50 g/L)
- the promoter profil activity for scrA is similar in a ΔscrR mutant than in the wild-type strain, in glucose, lactose or sucrose (whatever their concentration)

- The sucrose transporter ScrA is necessary for growth in LMD-9 strain in presence of glucose or sucrose as a single carbon source (no growth in a ΔscrA mutant)
 - ScrA is responsible for the transport of glucose and sucrose in LMD-9 strain
 - An explanation for the effect of glucose on scrA promoter activity modulation?



Conclusions

- S. thermophilus* is able to co-consume several sugars when mixed
- Carbohydrate metabolism regulation principally involves lactose and sucrose transporter gene expression via the general regulator CcpA
- Regulatory profiles for lacS and scrA genes according to sugar concentration and glycolytic flux are similar in LMD-9
- Catabolic repression in *S. thermophilus* LMD-9 does not strictly represses the consumption of less preferred sugars; instead, saccharides are jointly consumed

References:

- Gasser et al. Co-utilization of saccharides in mixtures: moving toward a new understanding of carbon metabolism in *Streptococcus thermophilus*, Int J Food Microbiol, doi 10.1016/j.fm.2022.104800
- Gasser et al, New insight on carbohydrate metabolism in *S. thermophilus*: role of sugar nature and concentration in operon regulation via carbon catabolite control, under review.