**Supplementary Table S1:** Integrative studies combining different omics approaches with respect to cheese flavor formation

| Cheese type | Aim of the study | Integrated methods applied | Microorganism/Metabolite | Correlation* | Reference |
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| Fiore Sardo<br>Pecorino Siciliano<br>Pecorino Toscano | Explore the effect of spatial distribution of metabolically active microbiota on secondary proteolysis and VOC production | 16S rRNA gene pyrosequencing and PT-GC-MS | *L. plantarum* | 2,4-hexadienal, benzaldehyde, methyl and branched esters (+) | [1] |
| | | | *S. thermophilus* | Acetaldehyde, propenal, 2,3-butanedione (+) | |
| | | | *Lactobacillus* sp. | aldehydes (n-alkanals, branched) (+)<br>some primary and secondary alcohols (+)<br>esters (methyl, ethyl, propyl, butyl, 1-methyl-propyl) (+)<br>sulfur compounds (dimethyl sulfide) (+) | |
| | | | *L. brevis* | 2,4-hexadienal, 3-heptanone (+) | |
| | | | *Brevibacterium* sp. | 14 esters, 9 aldehydes, 2 alcohols, 4 ketones, and 2 sulfur compounds (+) | |
| | | | *Brachybacterium* sp., *Arthrobacter*, *Halomonas variabilis* | aldehydes (2-heptenal), alcohols (1-hexanol), esters (propyl butanoate), ketones (2,3-octanedione) and sulfur compounds (2-methyl-tetrahydro-thiophen-3-one) (+) | |
| Caciocavallo Silano | Investigate the effect of increasing ripening temperature on microbial metabolism and | 16S rRNA pyrosequencing, shotgun metatranscriptome sequencing and SPME-GC-MS | NSLAB | 3-Methyl-1-butanol, volatile short-chain fatty acids (Butanoic acid, Pentanoic acid, Hexanoic acid, Heptanoic acid, Decanoic acid), 2-Nonanone, Nonanal | [2] |

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| | cheese maturation rate | | *L. casei, L. buchneri, L. plantarum, L. gasseri, L. fermentum, L. rhamnosus, Leuconostoc kimchii, Leuc. mesenteroides, Leuc. citreum, Pediococcus pentosaceus* | Increased amino acid metabolism activity | |
| Kazak | Analyze microbiota succession and flavor development during Kazak artisanal cheese ripening | 16S V4 / ITS amplicon sequencing and PT–GC-MS | *Acetobacter, Lactococcus, Bacillus, Staphylococcus* | 2-nonanone, acetoin and benzaldehyde (+) | [3] |
| | | | *Escherichia-Shigella*, *Moraxella* | Acetoin (+) | |
| | | | *Lactobacillus* | 1-hexanol, 2-heptanone, 2-nonanol, benzyl alcohol, hexanoic acid ethyl ester, nonanoic acid ethyl ester, octanoic acid ethyl ester (-) | |
| | | | *Kluyveromyces* | Butanoic acid, ethyl ester (+)<br>Heptanal (-) | |
| | | | *Aspergillus* | Heptanal, n-decanoic acid (+) | |
| | | | *Issatchenkia* and *Candida* | 3-methyl-1-butanol, ethyl acetate, phenylethyl alcohol, 2-methyl-propanoic acid (-) | |
| | | | *Issatchenkia* | n-decanoic acid (+) | |
| | | | *Candida* | Hexanoic acid (+) | |
| Cheddar cheese curd surface-ripened using commercial | Examine microbial succession and flavor development on the rind in | Whole-metagenome shotgun sequencing and HS-SPME GC-MS | *Debaryomyces hansenii* | Carboxylic acids and alcohols (+) | [4] |

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| smear-culture mixes | surface-ripened cheese | | *Glutamicibacter arilaitensis* | 3-methyl-1-butanol, phenylethyl alcohol, branched carboxylic acids, 2-heptanol, ketones (+) | |
| | | | *Brevibacterium linens* and *Geotrichum candidum* | Sulfur compounds, 2-methyl-1-butanol (+) | |
| | | | *Staphylococcus saprophyticus* | Ketones, esters, acids, and alcohols (+) | |
| | | | *Staphylococcus xylosus* | Sulfur compounds, 2-methyl-1-butanol, some ethyl esters (+) | |
| | | | *Corynebacterium variabile* | Ketones (+) | |
| Lab-scale mini-cheese smear-ripened with a culture of *Debaryomyces hansenii*, *Brevibacterium aurantiacum* and *Hafnia alvei* | Characterize metabolic interactions in a microbial synthetic cheese-ripening community | Microbial enumeration, UHPLC-MS, HPLC-UV, dual RNA-seq | *H. alvei* | Encodes a gene cluster for siderophore biosynthesis, increasing thus iron availability for *B. aurantiacum*<br>Increases sulfur amino acid availability for *B. aurantiacum* | [5] |
| | | | *B. aurantiacum* | Lipolysis of triglycerides from *B. aurantiacum* increases glycerol concentration in cheese, serving as energy substrate for *H. alvei*<br>Proteolysis of caseins from *B. aurantiacum* increases nitrogen availability for *D. hansenii* and *H. alvei,* while proteolytic activity of *B. aurantiacum* and other cheese microorganisms increased methionine catabolism in *H. alvei*, producing methanethiol | |
| *Macrococcus caseolyticus* subsp. *caseolyticus* | Explore the metabolic potential of *Macrococcus caseolyticus* subsp. | Whole genome sequencing and HS-SPME GC-MS | *Macrococcus caseolyticus* subsp. *caseolyticus* strains of dairy and non-dairy origin | Analysis of proteolytic and lipolytic systems components, strains' volatile profile when grown in lactose-free milk, association with FFA metabolism | [6] |

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| | *caseolyticus* to contribute to flavor formation | | | | |
| Artisanal and industrial cheddar cheese | Determine microbiota-metabolome relationships of artisanal and industrial cheddar cheeses | 16S rRNA amplicon sequencing, untargeted GC-MS, and LC-MS metabolomics | *Macrococcus* | 13 metabolites including two dipeptides and proline, in industrial cheeses (surface) | [7] |
| | | | *Lactobacillus* | Asparagine, proline, lysine, asparagine-valine, in industrial cheeses | |
| | | | *Pediococcus* | 21 metabolites including 1-formyl-pentadioic acid, a branched chain fatty acid (BCFA), in artisanal cheeses | |
| | | | *Streptococcus* and *Lactobacillus* | 3-hydroxy propanoic acid **only** in artisanal cheeses (+) | |
| | | | *Streptococcus* | O-Methoxycatechol O-sulphate in artisanal cheeses (surface) (+) | |
| | | | *Streptococcus* and *Lactobacillus* | 5-amino valeric acid, GABA, tyramine, in artisanal cheeses (core and surface) | |
| Commercial industrial cheddar cheeses of different ripening ages made by different manufacturers | Identify key microbiota and/or metabolite profiles of retail industrial cheddar cheeses of varying maturity and determine microbiota - metabolites interrelationships | 16S rRNA amplicon sequencing, and untargeted GC-MS metabolomics | *Thermus* in brand A | Phenylalanine (+) | [8] |
| | | | *Streptococcus* in brand B | Urea and lactose (-) | |
| | | | *Streptococcus* in brand C | Cholesterol and urea (-) | |

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| | | | *Lactococcus* in brand B | Heptadecanoic acid (+)<br>Urea (+) | |
| | | | *Lactococcus* in brand C | Pyroglutamic acid and piperidine (-)<br>Tyrosine (+) | |
| | | | *Lactobacillus* in brand C | Ornithine and glutamine (-) | |
| Similar-style cheddar cheeses of different qualities made by the same manufacturer | Determine microbiota and/or metabolite signatures (biomarkers) that could be used to assess cheese quality | 16S rRNA amplicon sequencing, and untargeted GC-MS metabolomics | *Streptococcus*<br>*L. lactis* | High-quality cheeses (+)<br>Low-quality cheeses (+) | [9] |
| | | | *Streptococcus* in high-quality cheeses | Aspartic acid, isoleucine, histidine, and proline (+) | |
| | | | *L. lactis* in low-quality cheeses | Stearic acid and octadecanol (+) | |
| Soft, semi-hard, and hard artisanal cheeses from Ireland together with publicly available cheese metagenomes | Assess the contribution of cheese microbiota to cheese quality | Meta-analysis of cheese microbiomes and corresponding volatilomes by GC-MS | Strain-level variation in species of *Brevibacterium linens*, *L. lactis* and *S. thermophilus* | Variations in volatile levels | [10] |
| | | | Metagenome-assembled genomes from putatively novel species | Acetate, succinate, lactate, and ammonium (+) | |
| Cheese curd agar inoculated with strains of the same three bacterial species, isolated from cheese rinds | Elucidate the impact of strain diversity across microbiomes from distinct geographic regions on community | Comparative genomics and HSSE-GC-MS | Cheese communities consisting of different strains of the same three species | Differing responses to abiotic (high salt) and biotic (the fungus *Penicillium*) perturbations, as well as variation in composition of VOCs emitted | [11] |

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| of different origin to construct synthetic microbial communities that mimic the microbial dynamics and functions of real surface-ripened cheese rinds | assembly dynamics and functional | | | | |
| 362 cheese rind samples collected from 137 different cheese types | Evaluate cheese microbiota diversity and functional potential | Amplicon and shotgun metagenomic sequencing | 14 bacterial and 10 fungal genera | Rind type (natural, washed, or bloomy) | [12] |
| | | | - | Genes involved in several metabolic pathways associated with flavor formation | |
| | | | *Pseudoalteromonas* spp. | Cold-adapted enzymes that participate in lipolysis and proteolysis | |
| Experimental surface-ripened cheese composed of nine microbial species | Explore the dynamics of the cheese microbial community, the metabolic activities of the different community members and their possible interactions during cheese ripening | Metagenomic and metatranscriptomic analysis | *L. lactis* and *K. lactis* | Expression of enzymes involved in lactose fermentation (+) | [13] |
| | | | *D. hansenii* and *G. candidum* | High levels of lactate dehydrogenase transcripts (+) | |

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| | | | *G. candidum* | Transcripts for proteolysis, lipolysis, and amino acid catabolism (+) | |
| Maasdam cheese ripened in different temperatures | Cheese microbiota characterization and gene expression during warm and cold room ripening | Metagenomic and metatranscriptomic analysis | *L. lactis* (subp. *lactis* or *cremoris*) | Genes for FFA biosynthesis, proteolysis, lipolysis, valine degradation and methionine-cysteine degradation (sulfur containing amino acids) | [14] |
| | | | *L. rhamnosus* | Genes for FFA biosynthesis, proteolysis, lipolysis, and methionine-cysteine degradation (sulfur containing amino acids) | |
| | | | *L. helveticus* | Genes for FFA biosynthesis, proteolysis, and methionine-cysteine degradation (sulfur containing amino acids) | |
| | | | *P. freudenreichii* subsp. *shermanii* | Genes for FFA biosynthesis, lipolysis, valine degradation and methionine-cysteine degradation (sulfur containing amino acids | |
| Historic Rebel cheese | Assess the biodiversity and richness of bacterial communities, the volatilome, terpenes and fatty acid profiles in HR cheese in order to characterize it | 16S rRNA gene sequencing, volatilome analysis by SPME GC-MS, terpene fraction and FA by Dynamic Headspace-Gas Chromatography-Mass Spectrometry (DHS-GC-MS) | *Lactococcus* | 3-Hydroxybutan-2-one, acetoin (+) | [15] |
| | | | *Leuconostoc* | Most ethyl-esters, ethanol, propionic acid (+) | |
| | | | *Lactobacillus* | 2-Heptanol (+) | |
| | | | *Streptococcus* | Hexanal, 1-hexanol (+) | |
| Pélardon cheese | Unravel bacterial and fungal dynamics during cheese | 16S rRNA and ITS gene sequencing. Volatile analysis by HS GC–MS | *L. lactis* and *L. mesenteroides* | Lactic acid, acetic acid, and 3-hydroxybutan-2-one (+) | [16] |

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| | preparation and ripening and determine their contribution in aroma production | | |
| | | *L. mesenteroides* | 3-methylbutanoic and 2-methylpropanoic acid (+) |
| | | *G. candidum* | 2-phenylacetaldehyde and 2-phenylethanol (+) |
| | | *L. paracasei, E. faecalis, P. commune, S. brevicaulis* | Ketones originating from FFA catabolism, responsible for strong "earthy" and "cheesy" notes |

*(+): Positive correlation; (-): Negative correlation

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