Facts

1. Individual features:
   1. Cells strongly prefer to sense and import nutrients or metabolites when available.
      * yeast would efficiently exploit the nutrients when available, to the extent that they solely rely on these extracellular metabolites [1].
      * Metabolic differences disappear between prototrophs and auxotrophs [2].
      * Prototrophic cells consumed histidine, leucine, methionine, and uracil at a comparable rate to the genetic auxotrophs, who depend 100% on external metabolite pools [1].
      * These changes reflect both downregulation and upregulation, indicating active metabolic adjustments in prototrophs that reflect their dual role of contributing and consuming metabolites​.
   2. Prototrophs growing alongside auxotrophs exhibit a different expression of enzymes involved in amino acid biosynthesis, compared to prototrophs growing among other prototrophs [3].
   3. Prototrophs both contribute and consume metabolites within SeMeCos [3].
   4. Prototrophs downregulated several metabolic enzymes in the presence of auxotrophs, indicating that they made use of metabolites released by the auxotrophs.
   5. Friendly component: Auxotrophs broadly reconfigure their metabolism and overflow metabolites other than those taken up when taking specific metabolites from the community [3]. Auxotrophs export metabolites that are not necessarily limited to the ones they require from their environment [3].
   6. Cells export relevant metabolites even when grown on minimal media [1].
2. Population composition:
   1. In SeMeCos two-thirds of the cells were auxotrophic for H, L, U or M [3].
   2. No auxotrophies were in a 1:1 ratio with each other (36.9% for uracil, 27.7% leucine, 23.7% histidine, and 11.7% methionine (Figure 2G right), despite the segregation rates predicting a relatively equal distribution, implying that selection pressure for certain metabotypes affected colony composition [1].
   3. 95.6% of cells belonged only to 8 of the 16 possible metabolic combinations [1].
   4. Spatial organization and physical contact are not limiting factors for metabolic cooperation to occur [1].
      * SeMeCo unequally distributse over the macroscopic structure, and form regions where the biosynthesis of a particular metabolite dominates.
      * Complementary metabotypes across the community maintained an average distance (6.86 mm) of less than two cell diameters.
   5. FBA predicted a faster growth rate of auxotrophs [3].
   6. MOMA, similar to community-extended FBA, predicted an increase in metabolite excretion [3].
3. Exometabolome composition
   1. 14 out of 20 extracellular metabolite concentrations (amino acids and uracil) were significantly increased [3].
   2. The presence of auxotrophs increases metabolite concentration in the community environment [3].
4. Evolution features
   1. Not all combinations of auxotrophic markers lead to the formation of successful cooperating cells [2].
      * Cooperation is not achieved in paired co-cultures (unlike bacteria).
      * Paired combinations of histidine (his3D), leucine (leu2D), uracil (ura3D), or methionine (met15D) auxotrophs were unable to sustain growth in the absence of supplementation required for both individual cell types [1].
   2. SeMeCo had adapted by maintaining a higher level of uracil in its exometabolome.
   3. SeMeCo colonies establish a population that is dynamic to changes in the external metabolite pool, and can persist in a state with virtually all cells being genetically auxotrophic for at least one essential metabolite [1].
   4. Metabolic feedback regulatory systems therefore do not inhibit metabolite export in general but prevent cooperative co-growth when already pre-established co-cultures are mixed.
   5. Grow potential and segregation do not explain the population composition
      * Cooperation is not a result of:
5. varying plasmid segregation rate
6. the number or type of auxotrophy: cells with one auxotrophy are found common or rear in the population.
7. differences in growth rates

Hypothesis

* Prevent the spread of foreign, potentially cheating: Metabolic feedback regulatory systems therefore do not inhibit metabolite export in general but prevent cooperative co-growth when already pre-established co-cultures are mixed (Mu ̈ller et al., 2014; Shou et al., 2007). A possible role of these mechanisms could perhaps prevent the spread of foreign, potentially cheating, cells that derive from a competing yeast colony. We could replicate behaviour which is in favour of such an assumption; By spiking into SeMeCo a cell culture possessing the same genotype as a frequent (HIS3 LEU2 ura3D MET15) and rare (his3D leu2D URA3 MET15) genotype (Figure 5A), we observed that both genotypes were rapidly depleted from the pre-established SeMeCo, irrespective of the frequency of the respective genotype in SeMeCo (Figure 5—figure supplement 1) [1].
* The role of these mechanisms could perhaps prevent the spread of foreign, potentially cheating, cells that derive from a competing yeast colony [1].
* Reduced genome size leads to faster proliferation [1].
* Cooperation is achieved progresively [2].
* Another possible explanation for the relatively stable coexistence observed in communities is that prototrophs might simply export or leak ‘costless’ metabolites. In this case the auxotrophic cells, even if cheaters, might impose minimal costs to the community because the metabolites essential to auxotroph 63 [3].
* Coordinated selection of metabolites: A key lesson to be learned from SeMeCos is that there are several metabotypes that do not make successful cooperators, while other combinations of the same auxotrophic alleles are compatible with effective cooperation [8]. One potential explanation for the latter is that all metabolite export, sensing and import is semi-selective. This means that although yeast cells release a broad spectrum of metabolites [6,10], as several belong to the same chemical category, such as aromatic or branched chain amino acids, they are therefore coordinately regulated, synthesized and transported [80,98]. Co-synthesis and co-transport hence puts constraints on the ability of cells to exchange connected metabolites independently from one another .
* metabolic dependency could drive community stabilization by distributing metabolic burdens [3]

References

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