

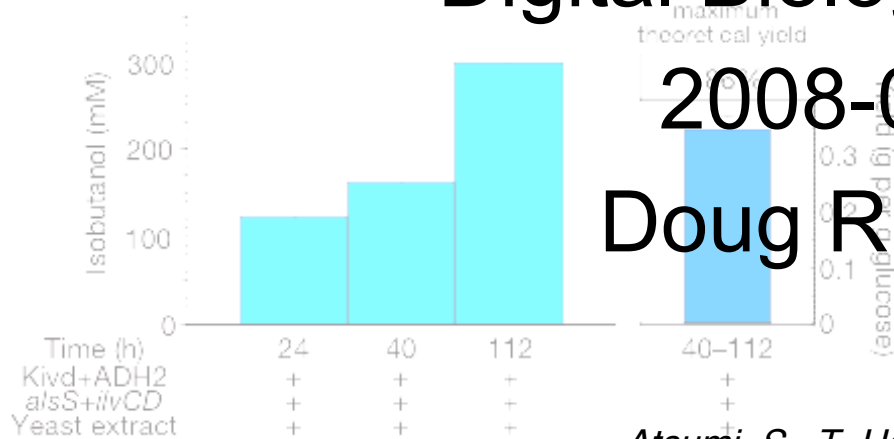
Novel biosynthesis of higher alcohols

Digital Biology Network

2008-01-30

Doug Ridgway

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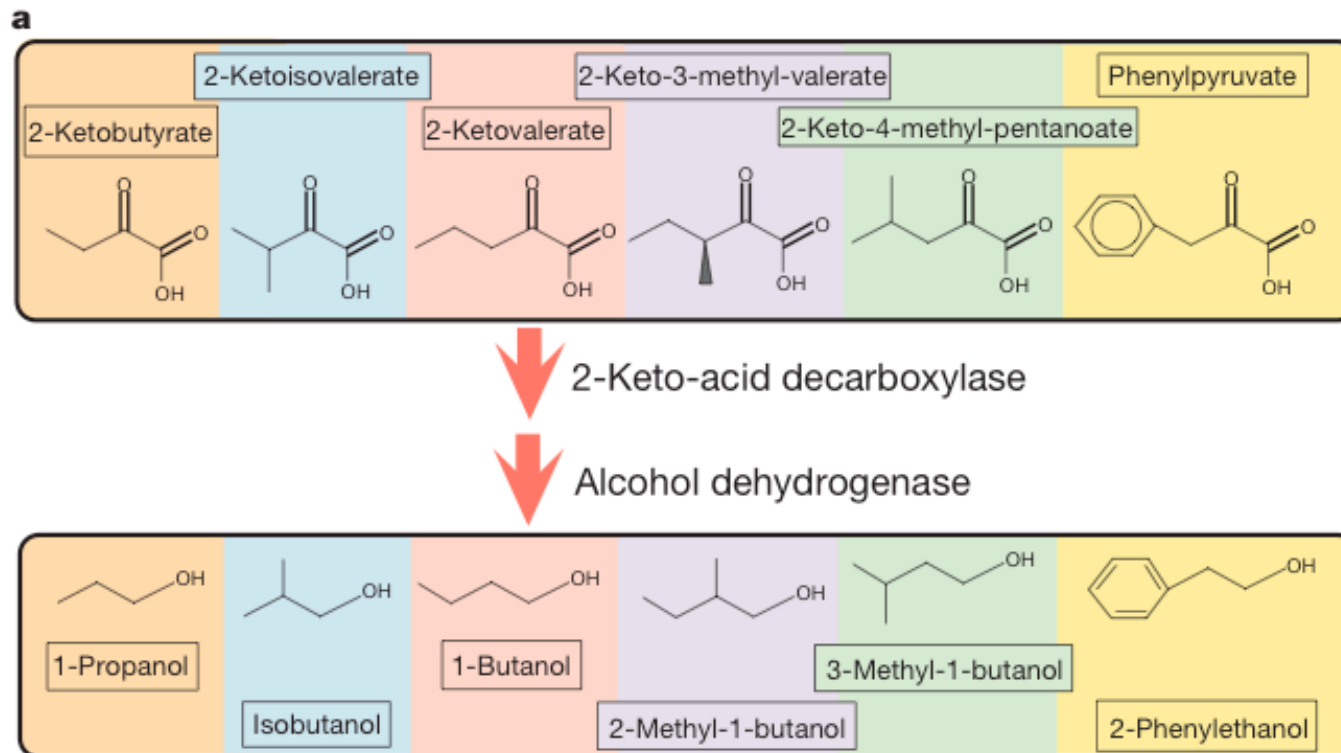


Atsumi, S., T. Hanai, and J. C. Liao. *Nature* 451:86-89 (2008)

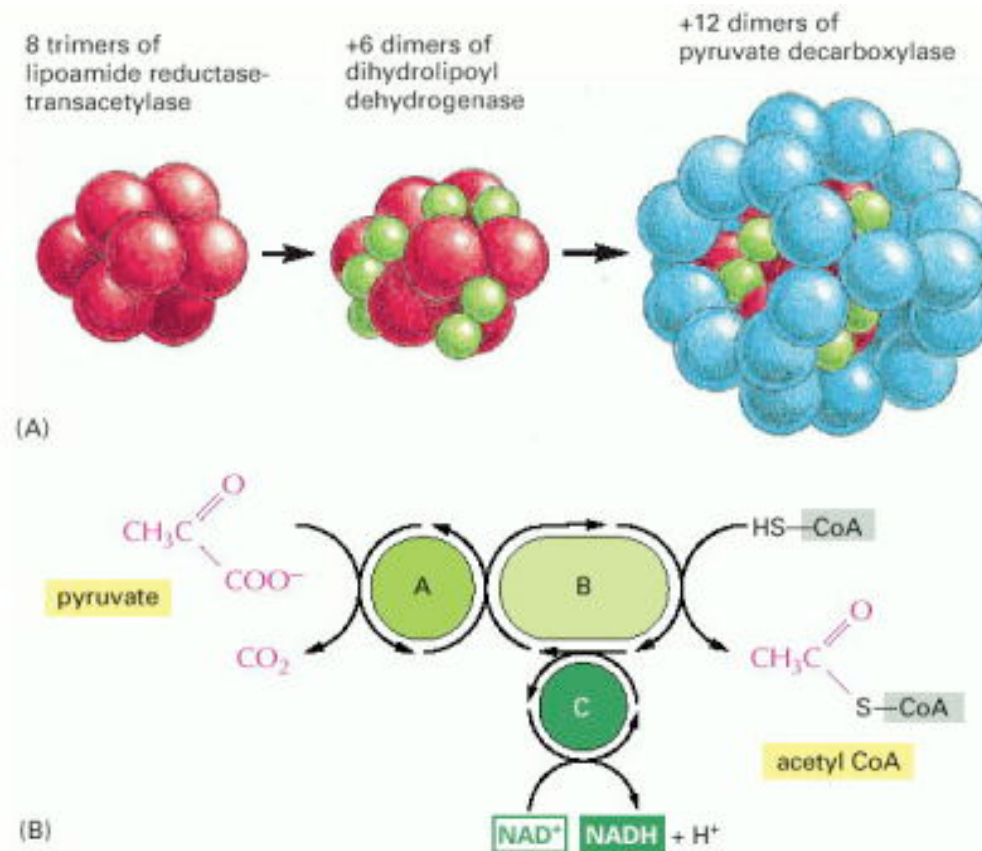
Why make higher alcohols?

- Better biofuels (energy density, and esp. hygroscopicity) than ethanol
- Useful solvents and platform chemicals
- Some may be less toxic than others
- Fun 'n easy

How do we make them?

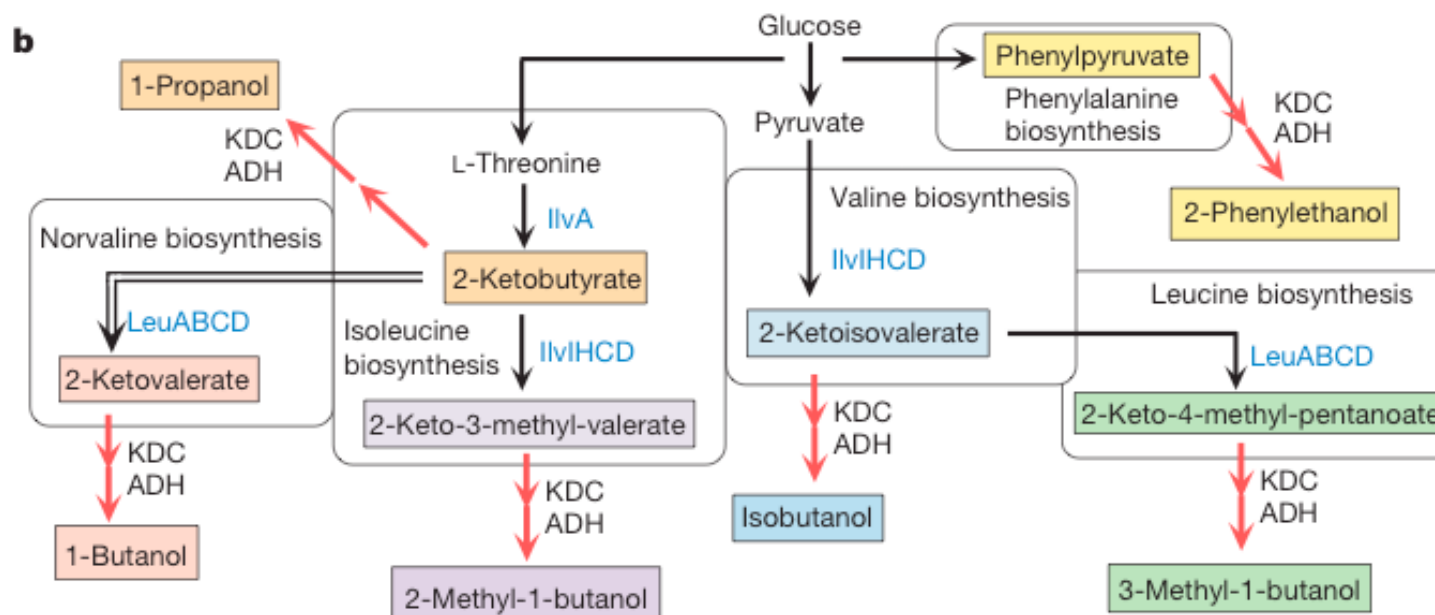


2-Keto acid decarboxylase



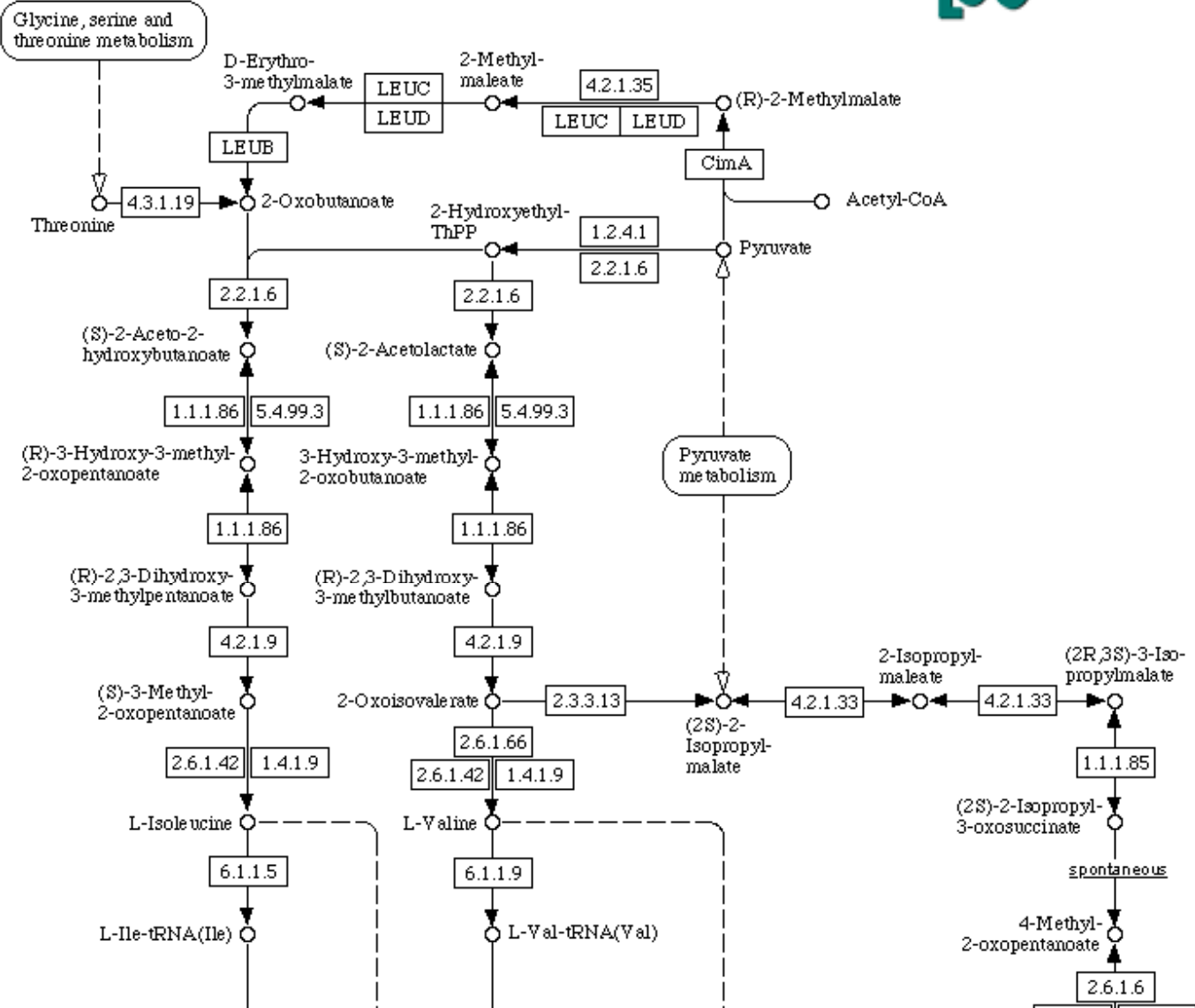
Tried 5, Kivd from *L. lactis* best

Where do we get the precursors?



Amino acid synthesis pathways

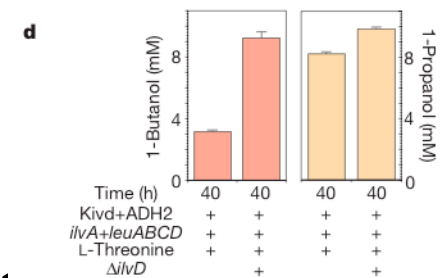
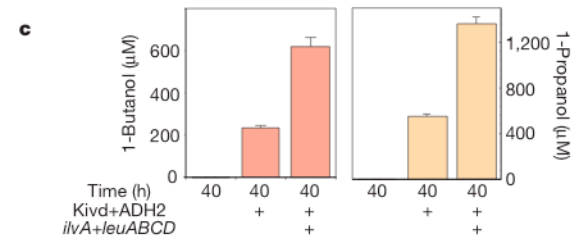
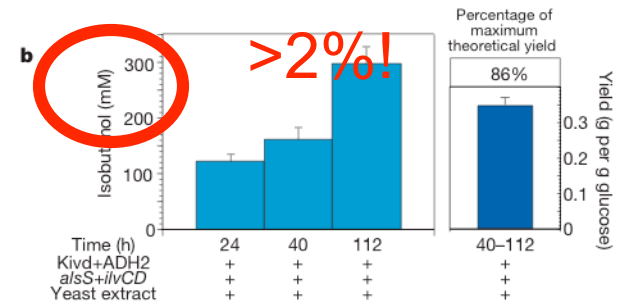
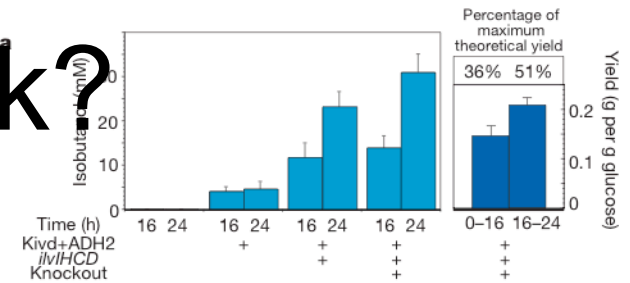
VALINE, LEUCINE AND ISOLEUCINE BIOSYNTHESIS



Does it work?

| Product (μM) | Kivd/pSA55 |
|---------------------------|------------|
| 1-Propanol | 520 |
| Isobutanol | 5,242 |
| 1-Butanol | 220 |
| 2-Methyl-1-butanol | 766 |
| 3-Methyl-1-butanol | 1,495 |
| 2-Phenylethanol | 324 |

First a little...

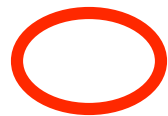
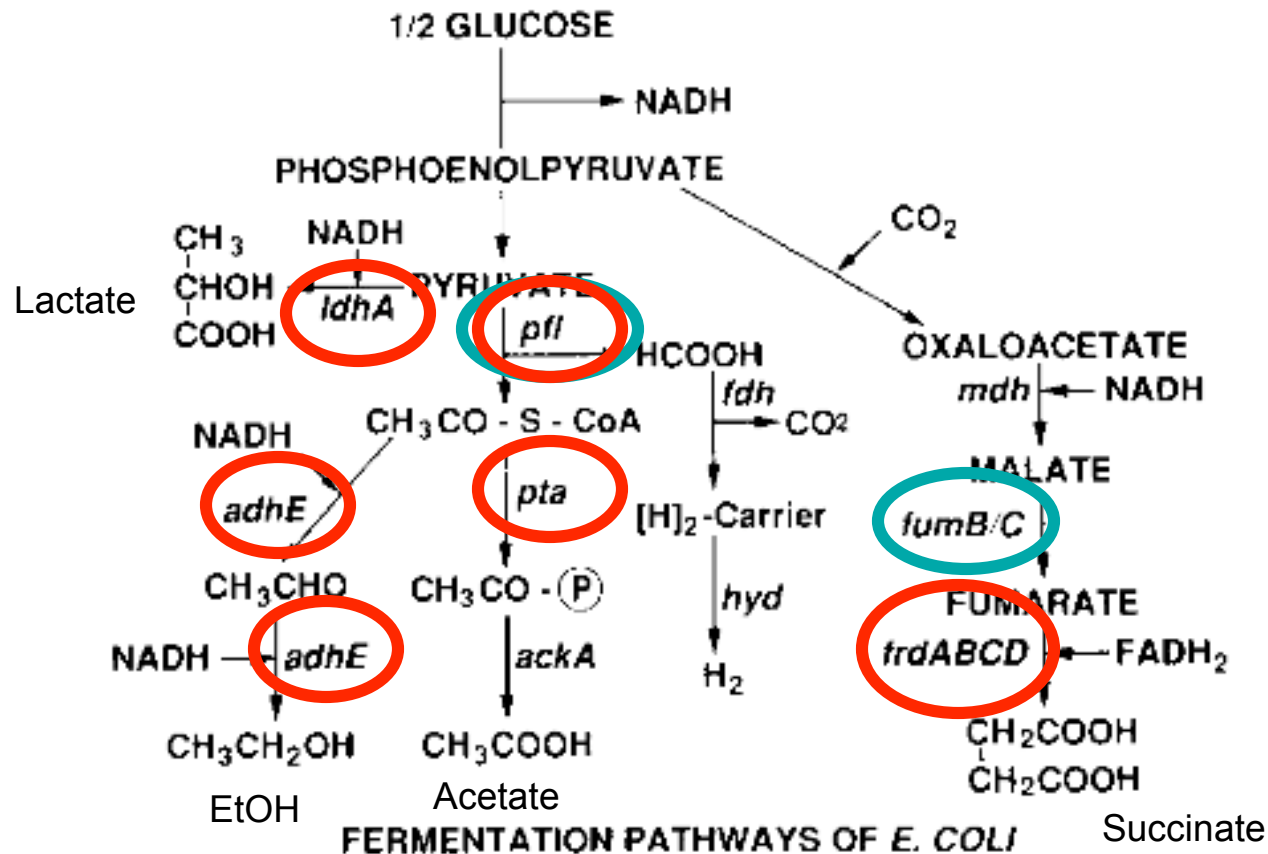


...then a lot.

Metabolic optimization

- \uparrow *ilvIHCD* -- valine, isoleucine pathways
- $\Delta adhE$, $\Delta ldhA$, $\Delta frdAB$, Δpta , Δpfl
 - fermentation product enzymes
- Δfnr -- activator for anaerobic respiration
- Replace *ilv* with *alsS* from *B subtilis*
- \uparrow cell density
- Microaerobic
- Then we get 2.2% isoBuOH

Avoiding side products



Deleted enzymes



Controlled by Fnr

Questions

- How do organisms expressing KDC avoid losing AA production to alcohols?
 - (hello, mitochondria!)
- Electron flow -- interesting to look at more/less reduced substrates
- What other nifty ideas didn't I think of...?

Generalize?

- Build db of existing metabolites and pathways (KEGG, metabolomes)
- Build db of known enzymes+reactions (esp incl nonspecifics)
- Compute exhaustive tree of possible products -- “bioproductome”
- Do market evaluations, select interesting targets