

## **Nitrogen metabolism in enteric bacteria**

Two intermediates: glutamate and glutamine

One precursor: 2-oxoglutarate

Glutamine is used to sense nitrogen availability

Glutamate is required to maintain the steady-state  $K^+$  pool

## **Circuitry from glutamine that allows coordinated slowing of growth under N-limiting conditions**

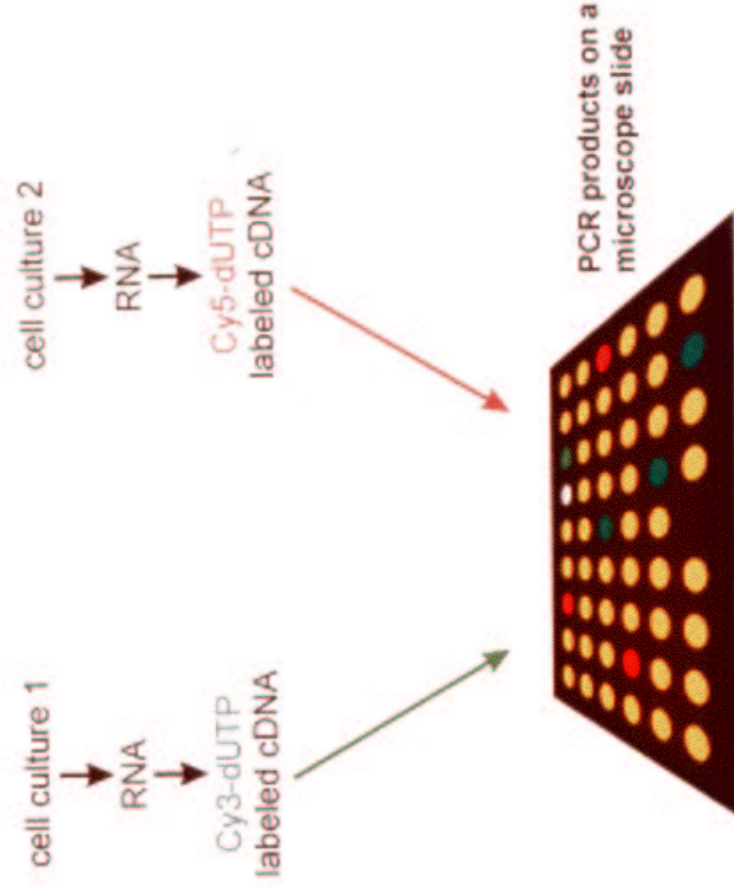
The amide group of glutamine is required directly for the biosynthesis of monomeric units of all macromolecules.

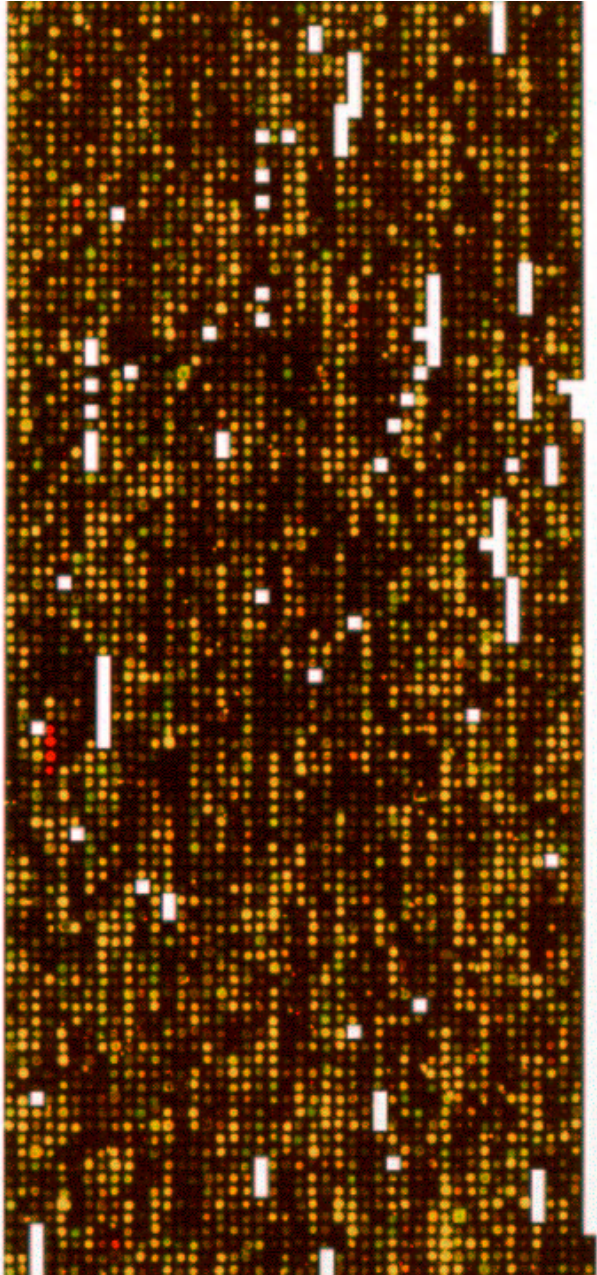
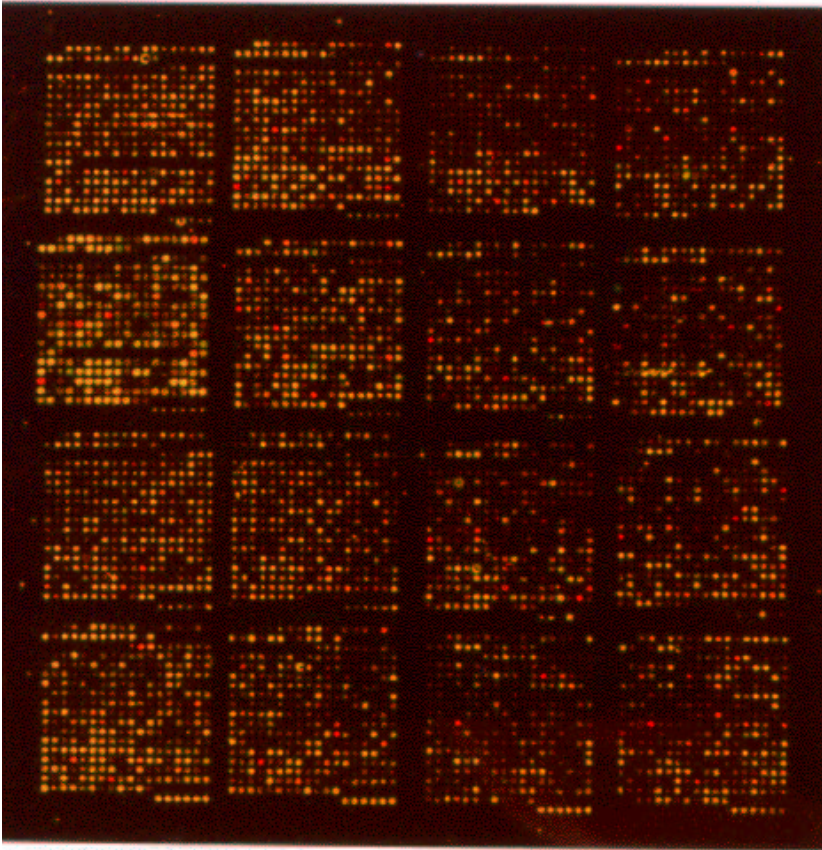
With the exception of the histidine biosynthetic pathway, glutamine is required at the first dedicated step of every pathway in which it is utilized.

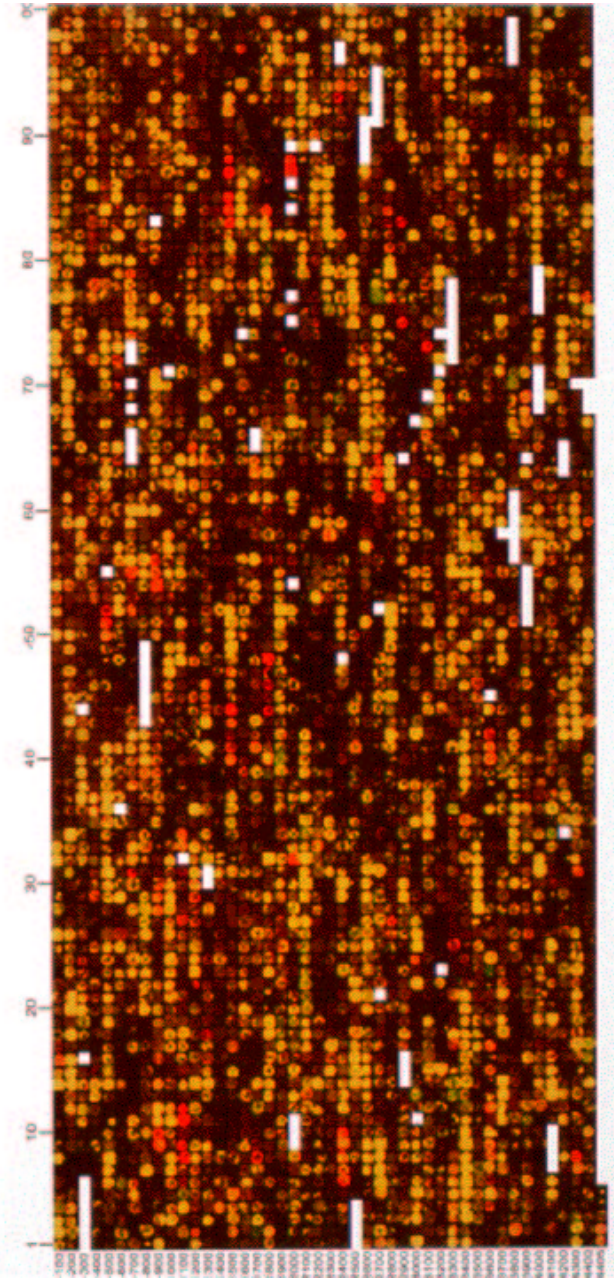
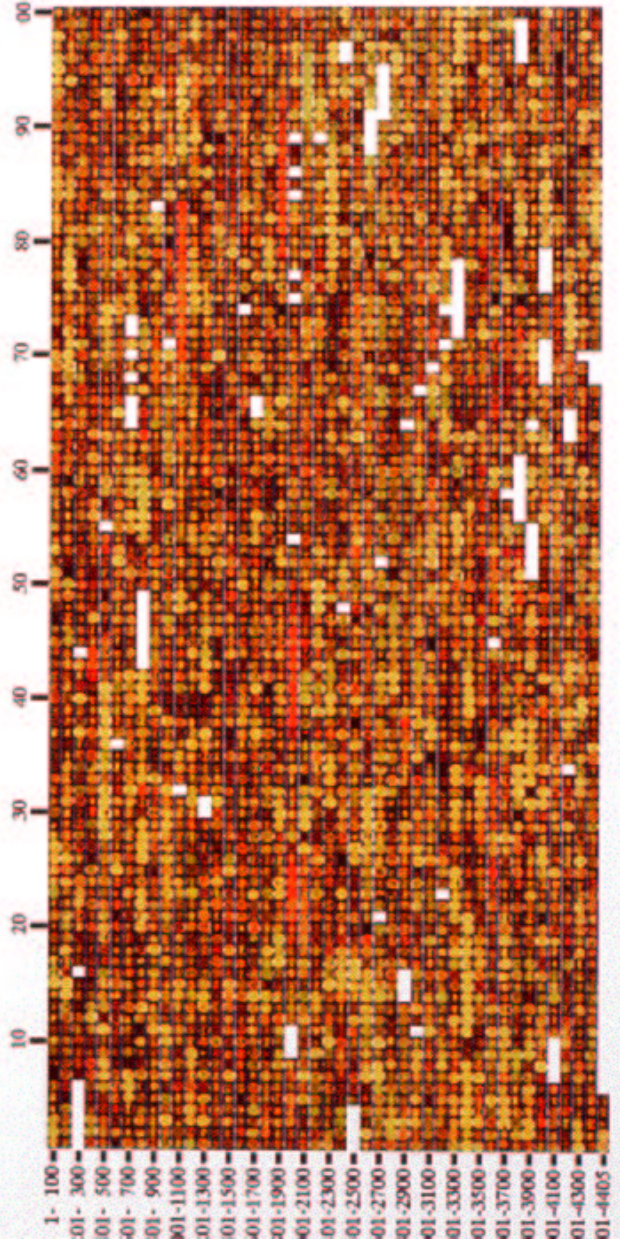
Glutamine-dependent reactions are generally coupled to ATF hydrolysis and cannot reverse to refill a depleted glutamine pool.

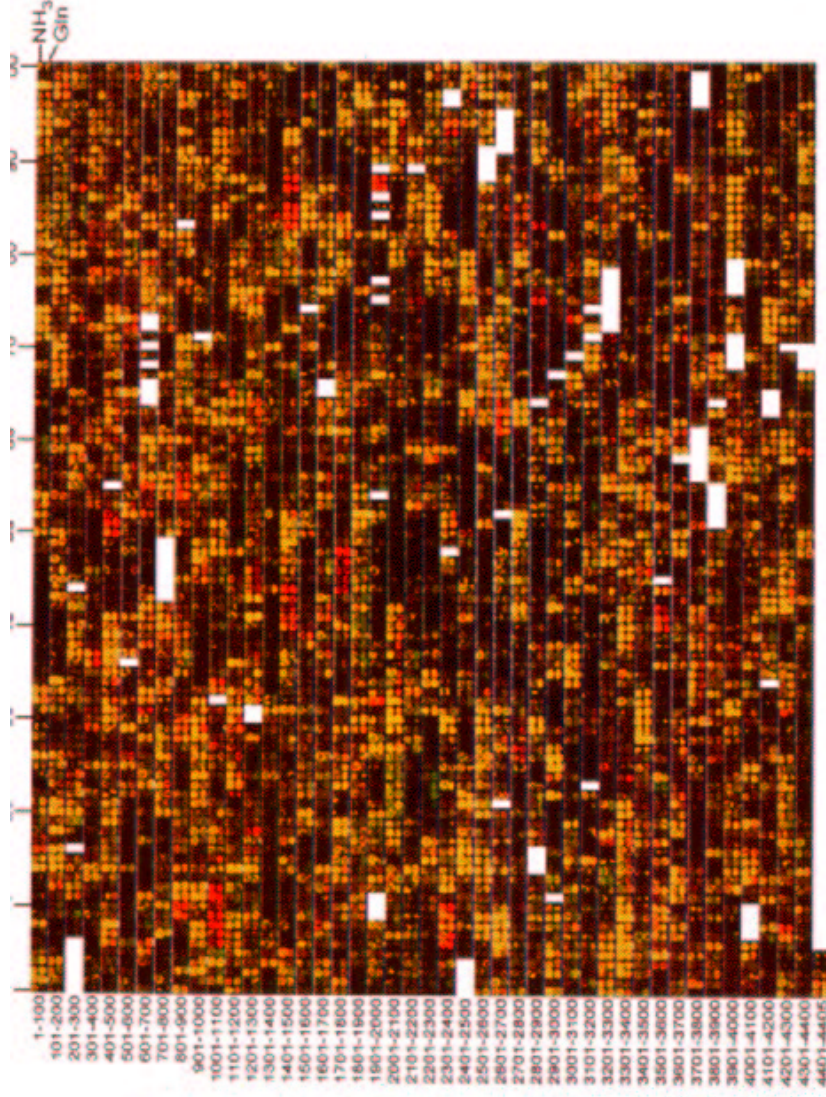
## Potential problems caused by low $K^+$ glutamate

- Loss of polyribosomes and defects in translation of mRNA into protein.
- Defects in cell wall synthesis.
- Problems due to tight protein-nucleic acid interactions.

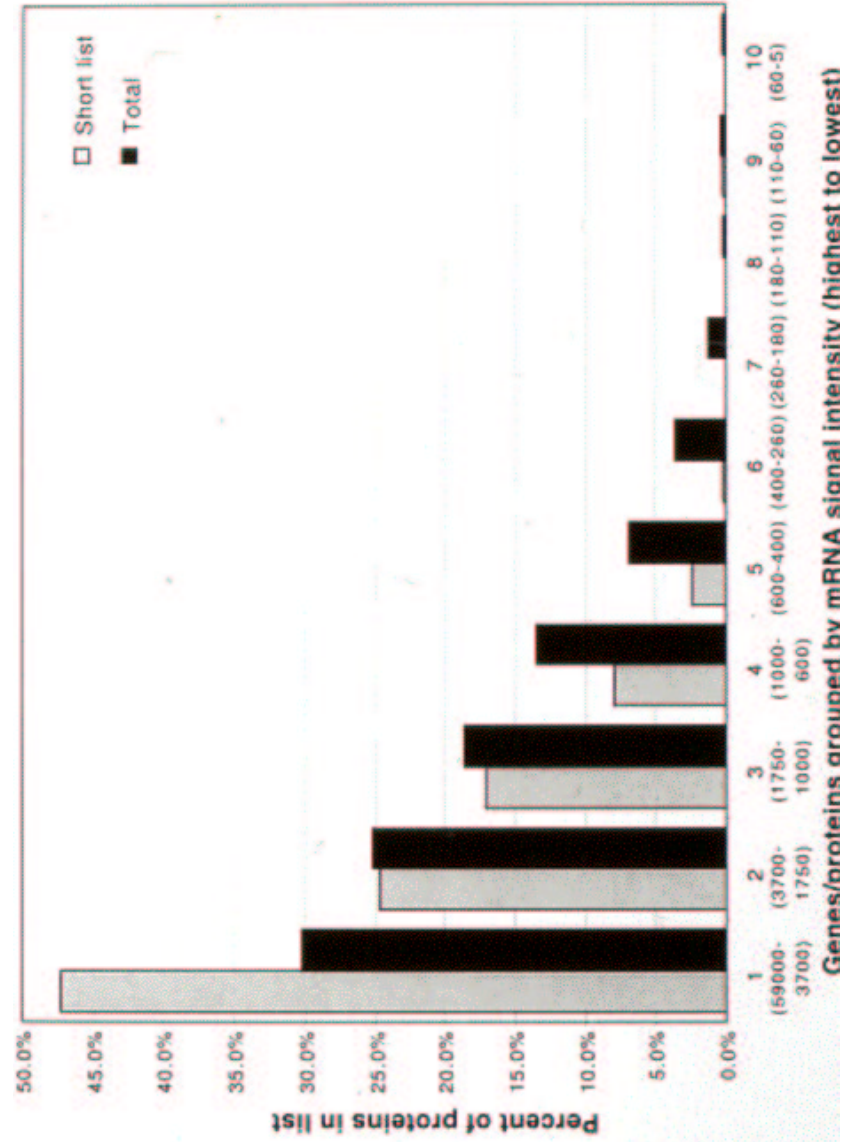
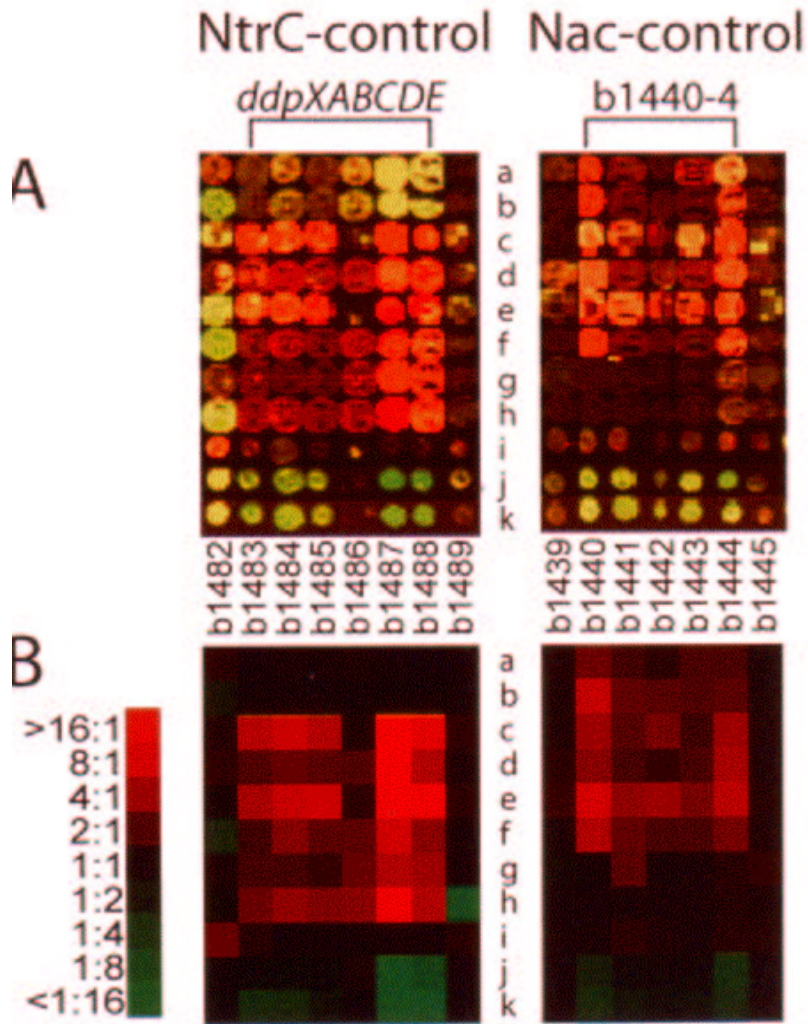


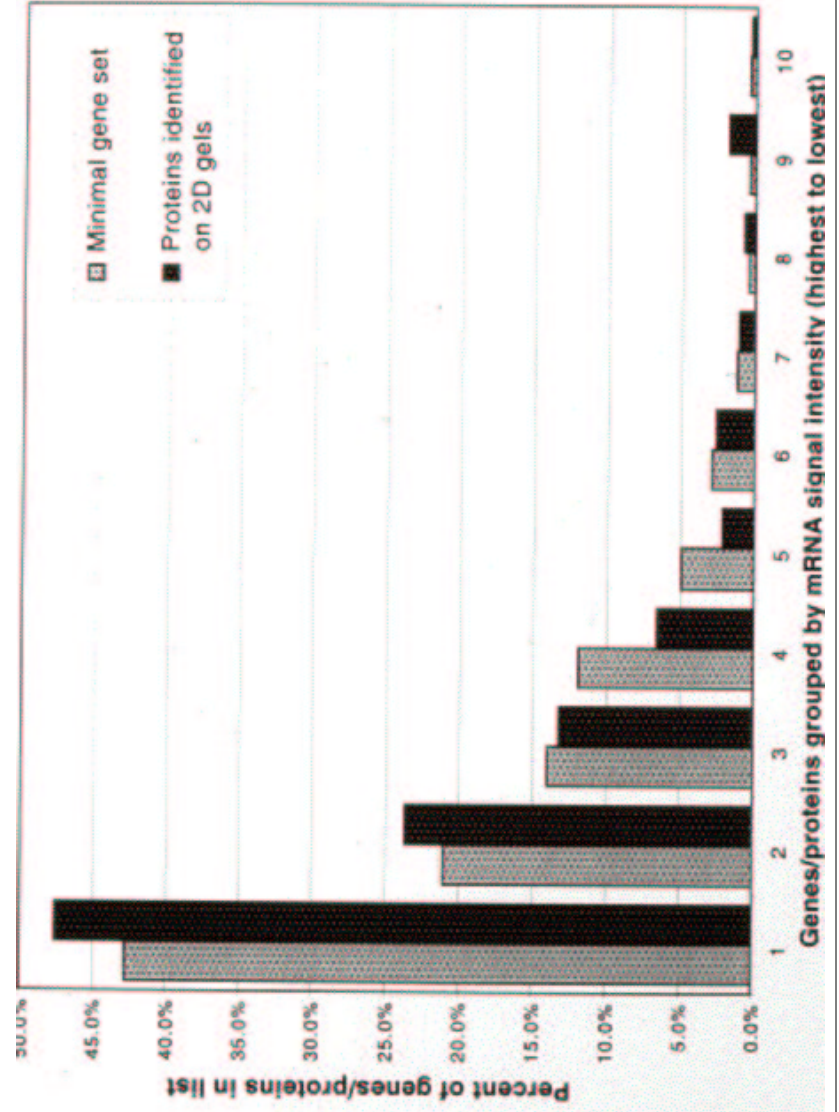
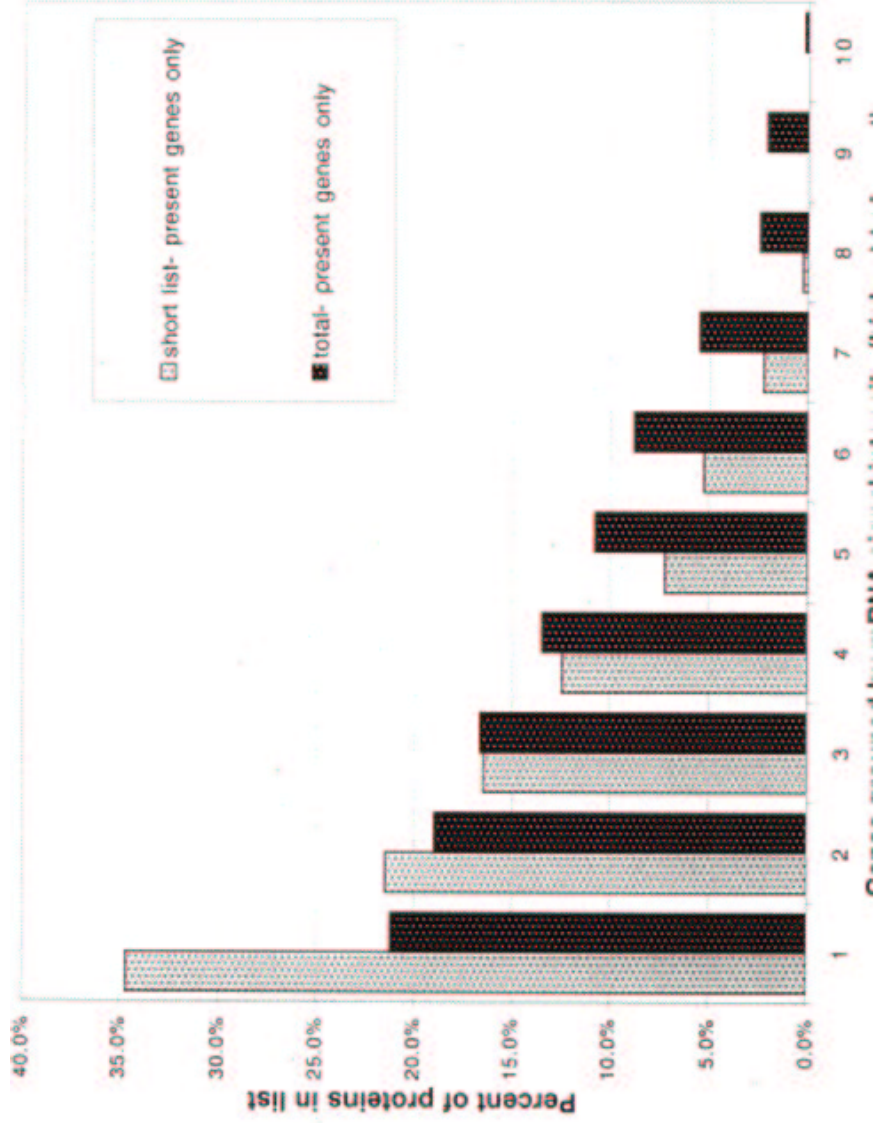




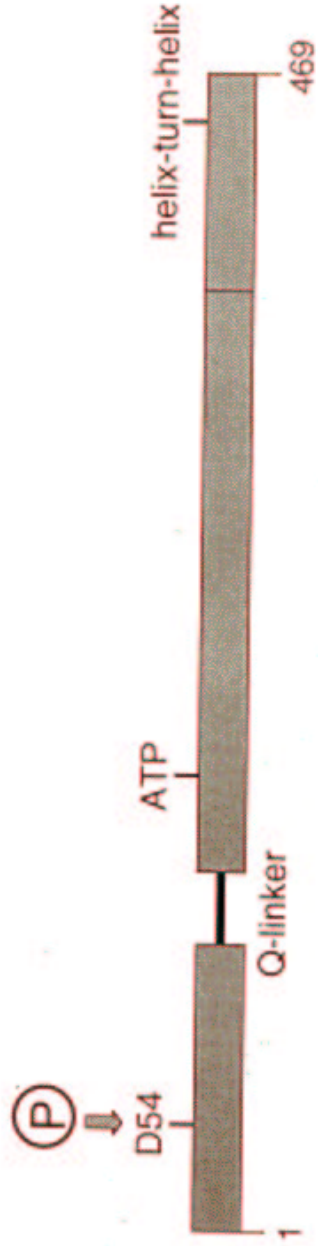


b#	Name	Description	Control
b0336-7	<i>codBA</i>	cytosine transport, deaminase	Nac
b0450-1	<i>glnK-amb</i>	N-regulation and NH <sub>3</sub> transport	NtrC
b0652-5	<i>gltJKL</i>	glutamate transport	NtrC?
b0809-11	<i>glnHPQ</i>	glutamine transport	NtrC
b0854-7	<i>potFGHI</i>	putrescine transport	NtrC
b0929	<i>ompF</i>	outer membrane protein F	Nac?
b1006-12	<i>ycdGHIJKLM</i>	hypothetical proteins	NtrC
b1217-8	<i>chaBC</i>	cation transport regulator	NtrC?
b1243-8	<i>oppABCDF</i>	oligopeptide transport	Nac?
b1440-4	<i>ycdSTUV</i>	putrescine/spermidine transport	Nac
b1483-8	<i>ddpXABCDE</i>	D-ala-D-ala dipeptide transport and dipeptidase	NtrC
b1744-8	<i>astCADBE</i>	arginine catabolism	NtrC
b1783-4	<i>ycgGH</i>	hypothetical proteins	NtrC?
b1932	<i>yedL</i>	hypothetical protein	Nac
b1987	<i>cbl</i>	regulator for sulfur metabolism	NtrC
b1988	<i>nac</i>	N-regulation	NtrC
b2306-9	<i>hisJQMP</i>	histidine transport	NtrC
b2310	<i>argT</i>	basic amino acid transport	NtrC
b2393	<i>nupC</i>	nucleoside transport	NtrC
b2661-4	<i>gabDTPC</i>	γ-aminobutyric acid transport and catabolism	Nac
b3073	<i>ygG</i>	probable ornithine aminotransferase	NtrC
b3268-71	<i>yhjWXYZ</i>	polar amino acid transport	NtrC
b3540-4	<i>dppABCDF</i>	dipeptide transport	Nac?
b3868-70	<i>glnALG</i>	NH <sub>3</sub> assimilation and N-regulation	NtrC
b4207-8	<i>flbB-cycA</i>	peptidyl-prolyl isomerase; D-ala,D-ser.gly transport	Nac





## Domain structure of NtrC

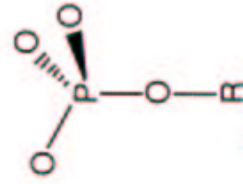


Regulation

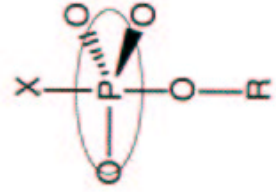
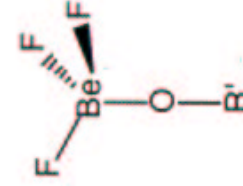
Transcriptional activation

DNA-binding

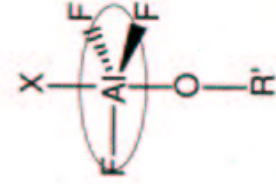
## Phosphate vs. its metal-fluoride analogs



ground state



transition state







Growth defect of an *amtB* mutant

	Doubling time (minutes)		
	pH 7	pH 5	
[NH <sub>4</sub> <sup>+</sup> + NH <sub>3</sub> ], mM	5	0.5	0.5
wild type	59	65	80
<i>amtB</i>	59	64	370

## The Rh blood group substance

Present at  $\sim 10^5$  copies/red cell

Function unknown for 6 decades

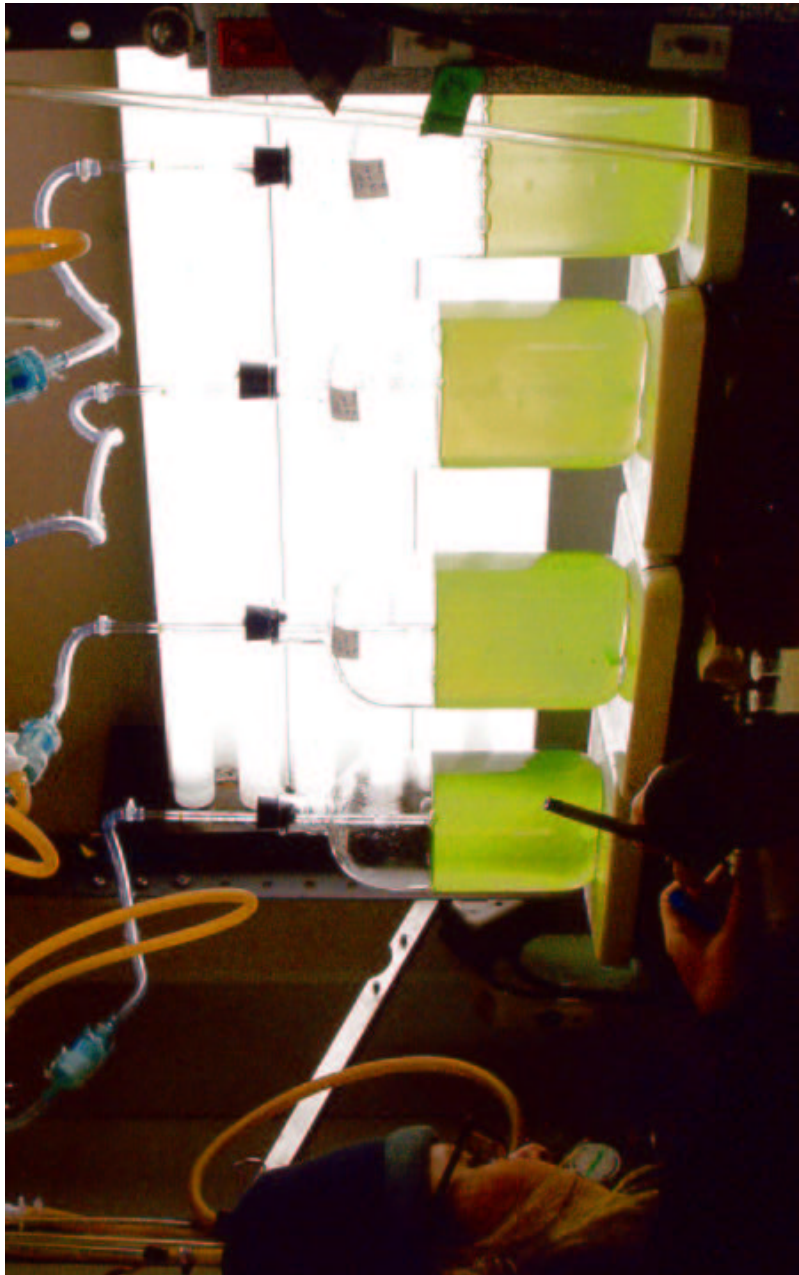
Only the  $\text{HCO}_3^-$  exchanger (band 3) and glycophorin A more abundant  
( $\sim 10^6$  copies/cell)

### Organismal distribution of Rh and Amt proteins

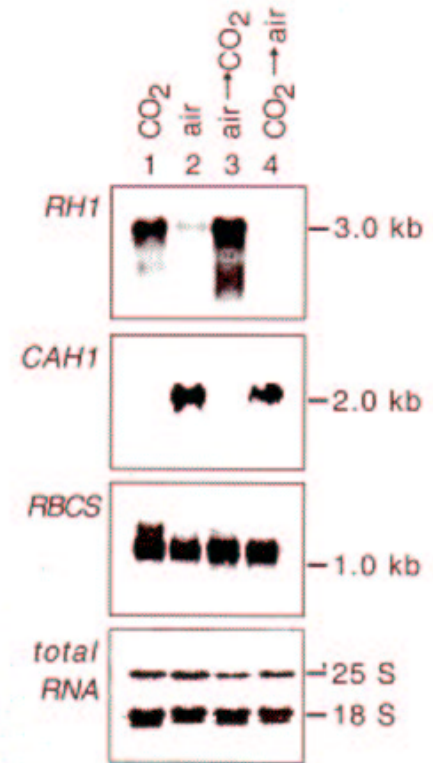
	Rh <sup>+</sup>	Amt
Bacteria	-	+
Archaea	-	+
Microbial eukarya	rare	+
Higher Plants	-	+
Invertebrates	+	+
Vertebrates	+	-

prominent in mammals\* absent in mammals

\* The RhAG and Rh30 proteins of humans and mice are found in erythrocytes. The RhBG protein is found in kidney (convoluted tubules and Henle's loops), skin, liver and ovary. The RhCG protein is found in kidney (collecting ducts), brain, pancreas, prostate, and testis (seminiferous tubules).  
[Liu et al. J. Biol. Chem. 275:25641-51 (2000)]  
Liu et al. J. Biol. Chem. 276:1424-33 (2001)]



**RH1 is highly expressed only at high CO<sub>2</sub> (3%)**



Erythroid lineage



RH negative  
RH null

lack D antigen  
lack all erythroid Rh antigens  
cytoskeletal abnormalities

Rh1 protein is highly expressed only at high CO<sub>2</sub>

