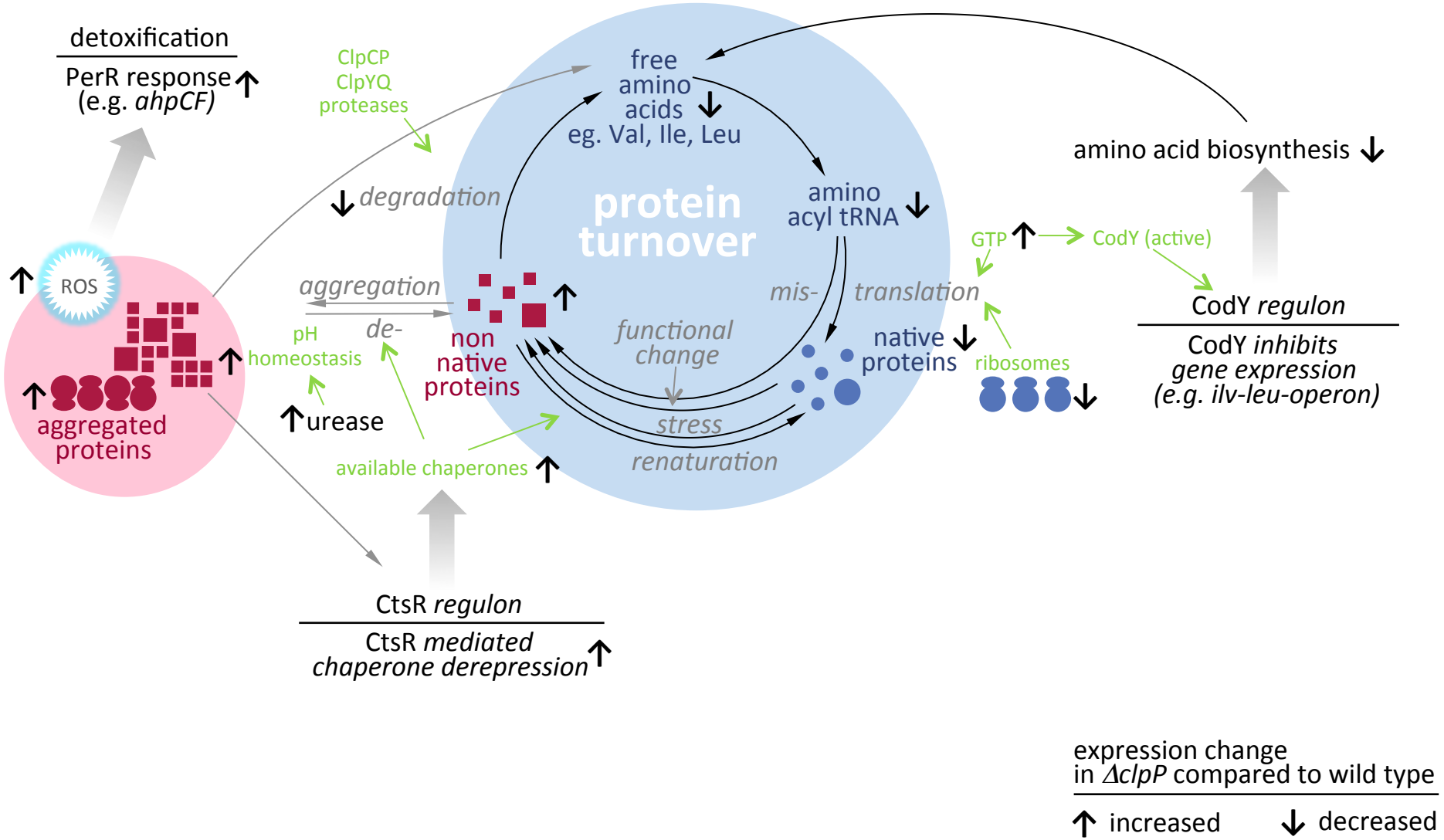
detoxification
PerR response
(e.g. ahpCF)
ClpCP
ClpYQ
proteases
free
amino
acids
eg. Val, Ile, Leu
protein
turnover
degradation
amino
acyl tRNA
amino acid biosynthesis
GTP
CodY (active)
CodY regulon
CodY inhibits
gene expression
(e.g. ilv-leu-operon)
ROS
aggregation
mis-
translation
native
proteins
ribosomes
aggregated
proteins
pH
homeostasis
de-
non
native
proteins
functional
change
urease
stress
renaturation
available chaperones
CtsR regulon
CtsR mediated
chaperone derepression
expression change
in ΔclpP compared to wild type
increased
decreased

Figure S15

Figure S15:

Schematic model of the mechanisms underlying the pleiotropic *clpP* mutant phenotype. Owing to the lack of *clpP* the mutant cells accumulate non-soluble proteins. Consequently, these proteins are no longer able to exert their function. This promotes a higher level of GTP in the cells due to the lower ribosomal activity, which results in a strong repression of CodY-regulated genes. The consequence is a low production of branched-chain amino acids due to low amounts of corresponding biosynthetic enzymes. This leads to a higher level of uncharged tRNA and result in a weak activation of the stringent response, with decreased expression of ribosomal proteins. In addition the protein stress / reactive oxygen species (ROS) production through the protein aggregation leads to a strong induction of the CtsR and PerR -regulons resulting in a high amount of chaperones and detoxification enzymes.