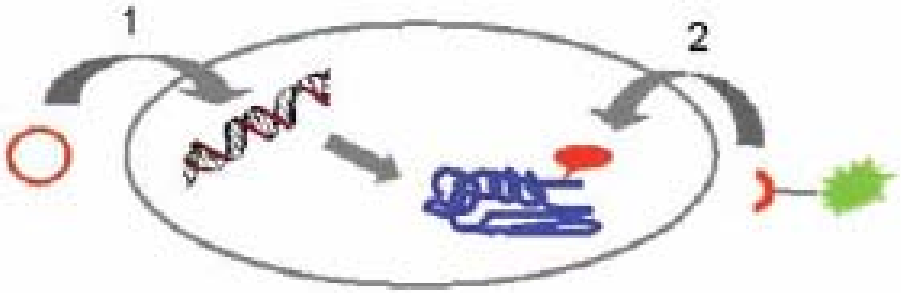
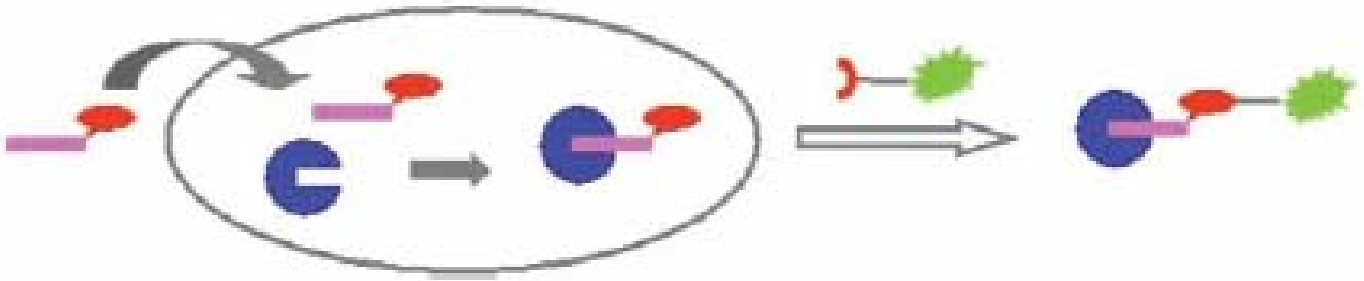
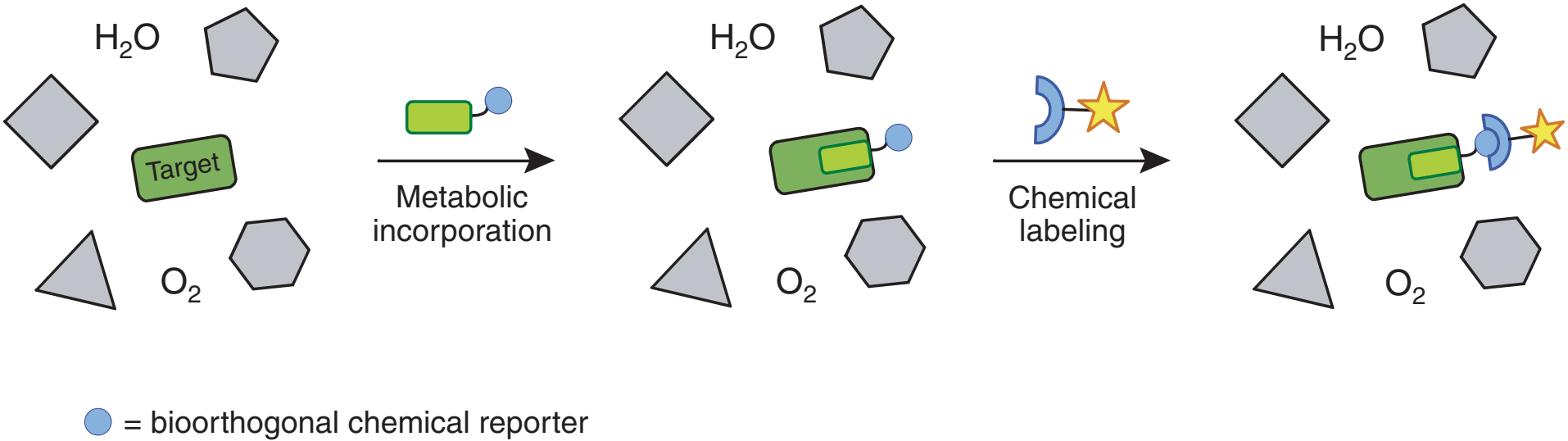
A.

B.



C.




H_2O
Target
O_2
Metabolic
incorporation
H_2O
O_2
Chemical
labeling
H_2O
O_2
= bioorthogonal chemical reporter

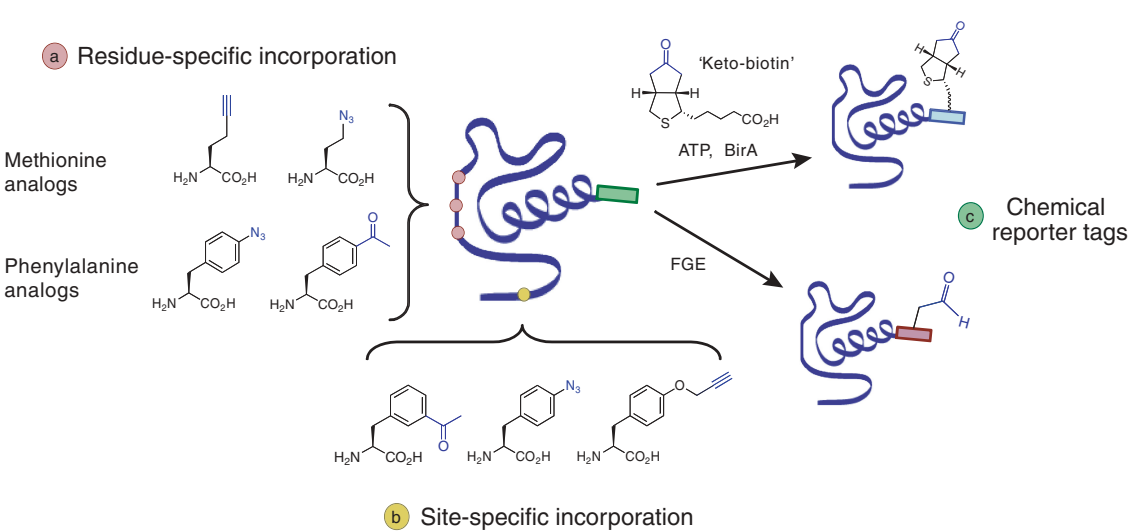
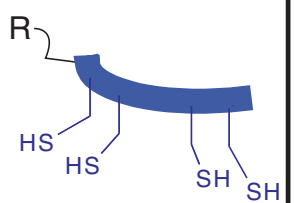
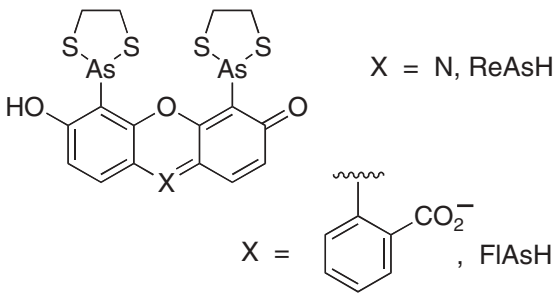
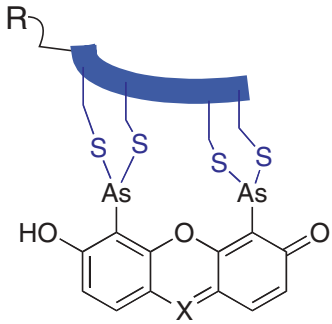
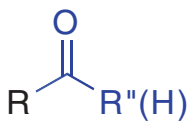
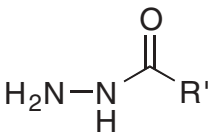
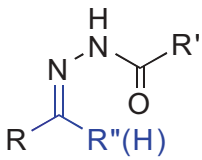
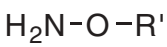
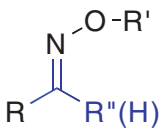
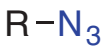
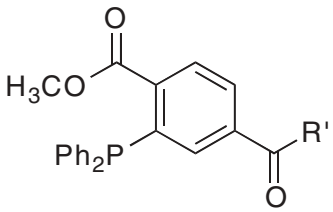
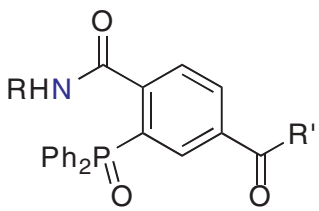
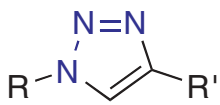
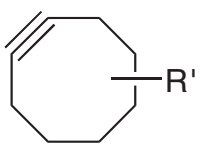
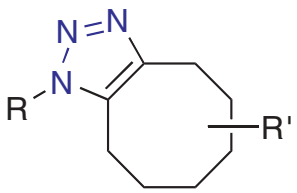
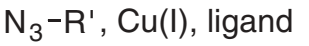
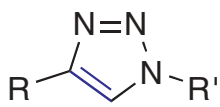
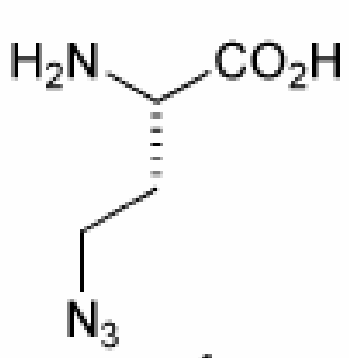

a Residue-specific incorporation
Methionine analogs
Phenylalanine analogs
'Keto-biotin'
ATP, BirA
FGE
c Chemical reporter tags
b Site-specific incorporation

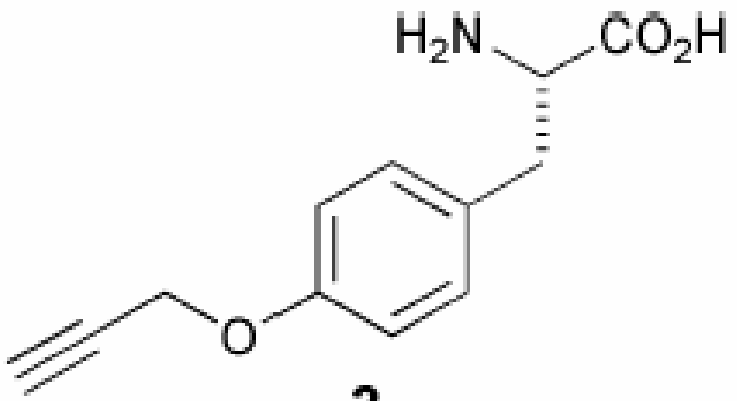
Table 1 Chemical reporters and bioorthogonal reactions used in living systems.

Chemical reporter	Reactive partner (R´ = probe)	Ligation product	Target[a] (R)
 Tetracysteine motif			Protein[18,31]
 Ketone/aldehyde			Protein[19,20] Glycan[22]
			
 Azide	Staudinger ligation 		Protein[17,26]
	‘Click’ chemistry 		Glycan[30,34] Lipid[25]
	Strain-promoted cycloaddition 		
 Terminal alkyne	‘Click’ chemistry 		Protein[29]

[a]Only literature examples provided. Other biomolecules could potentially be labeled in a similar manner.



1



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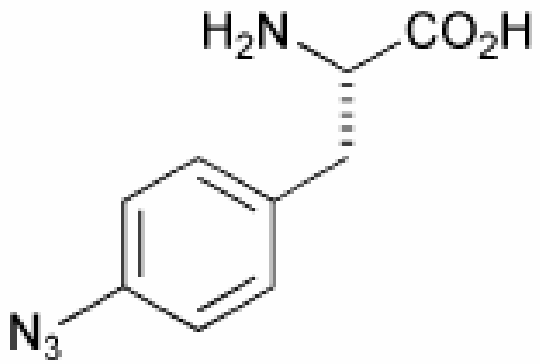
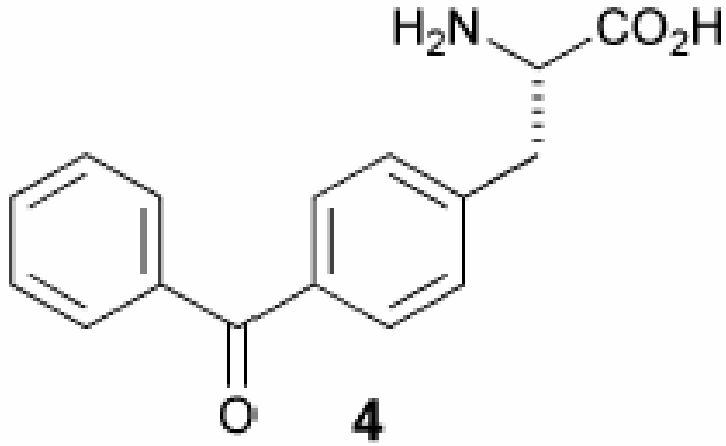


3



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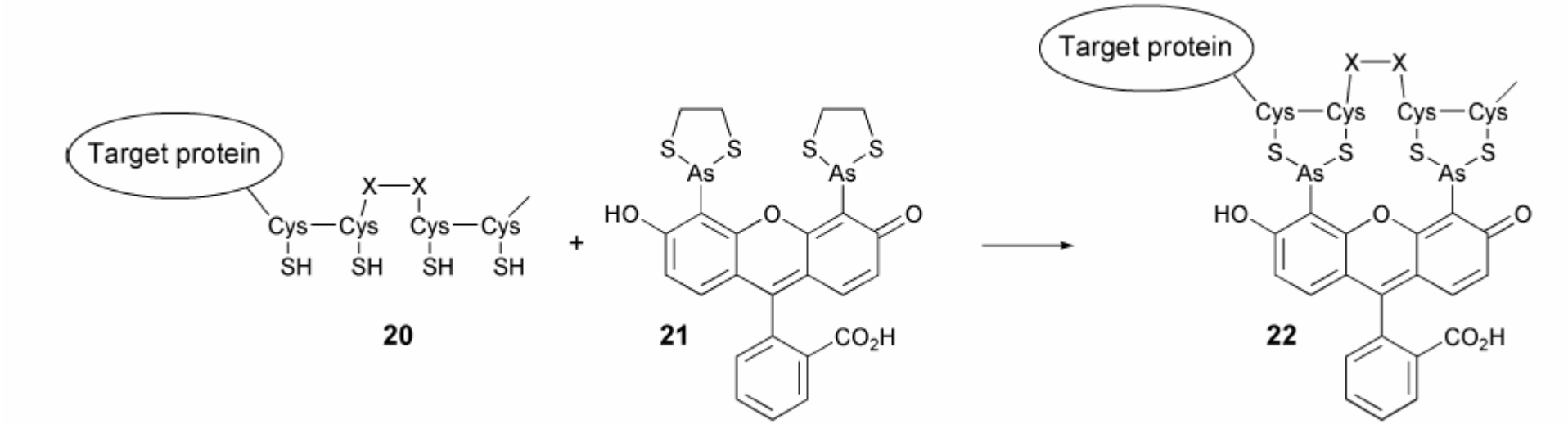
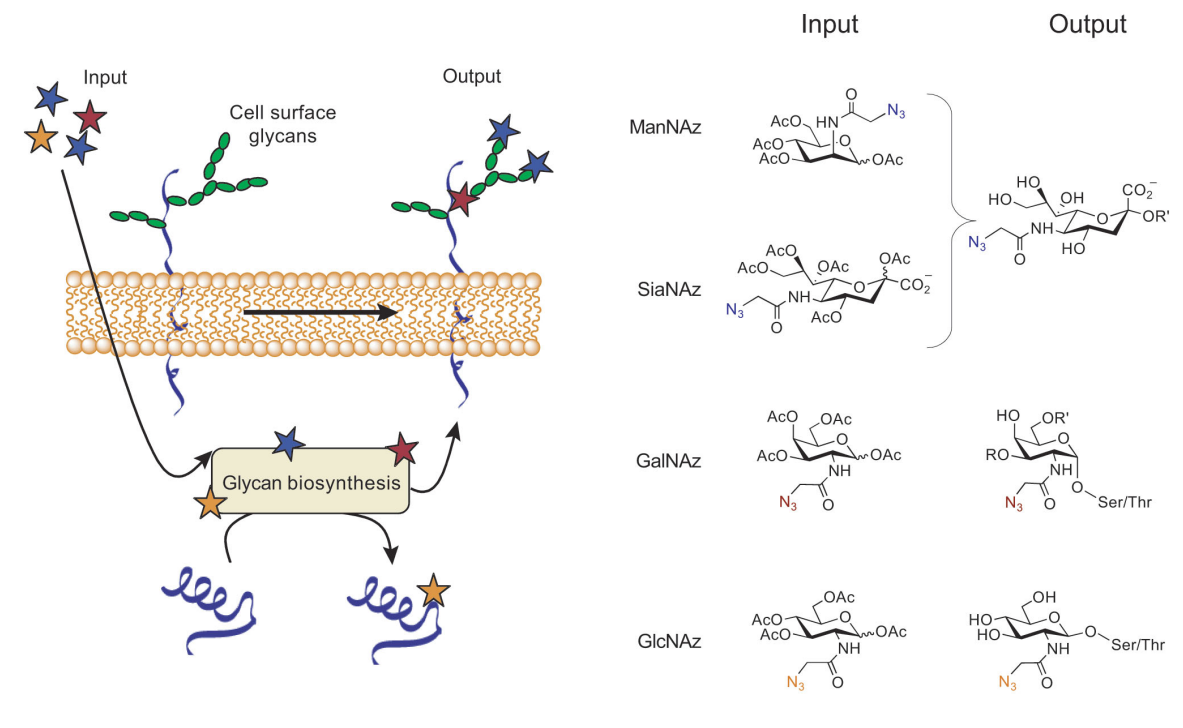

Target protein
X—X
Cys—Cys Cys—Cys
SH SH SH SH
20
+
S S
As
S S
As
HO
O
O
CO2H
21
Target protein
X—X
Cys—Cys Cys—Cys
S S S S
As As
HO
O
O
CO2H
22


Input
Output
Cell surface glycans
Glycan biosynthesis
Input
Output
ManNAz
SiaNAz
GalNAz
GlcNAz
Ser/Thr
Ser/Thr