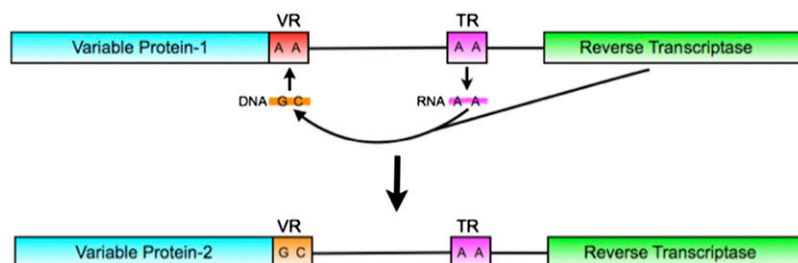
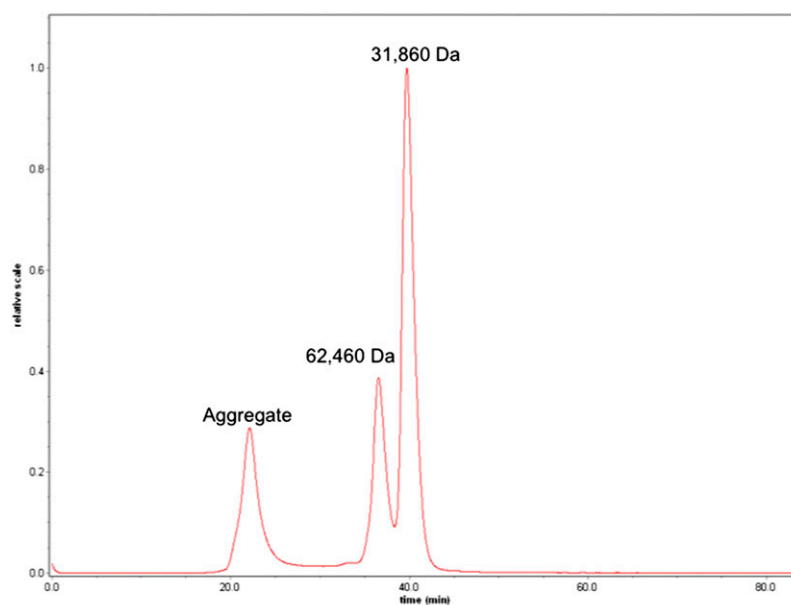


# Supporting Information

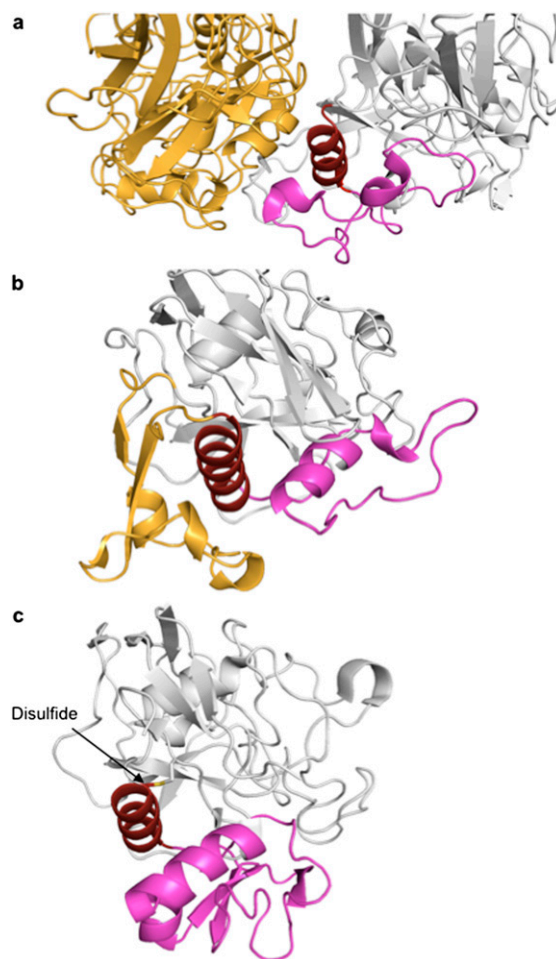
Le Coq and Ghosh 10.1073/pnas.1105613108



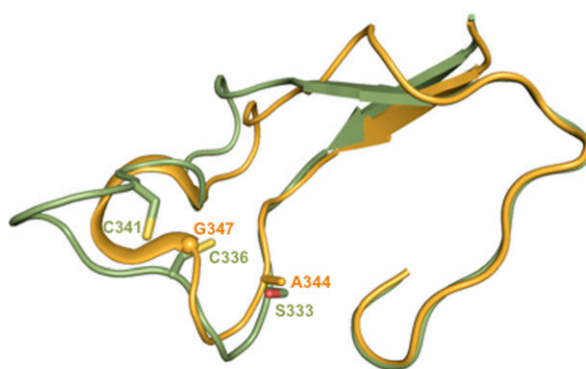
**Fig. S1.** Diversity generation. Genetic information is transferred from the invariant TR to the protein-encoding the VR at the C terminus of the DGR-variable protein through the action of the DGR reverse transcriptase on TR RNA. Two adenines in the TR are shown to be randomly mutated to other bases (G and C here) and incorporated into the coding locus of the variable protein to give rise to a new variant.



**Fig. S2.** Size-exclusion profile of TvpA. The molecular masses determined for TvpA by static light scattering of peak fractions are indicated. The calculated molecular mass of TvpA is 32,136 Da.



**Fig. 53.** The role of insert 1'. (A) Ribbon representation of one of the protomer–protomer interfaces in trimeric Mtd. The gray protomer has the  $\alpha$ 1 helix in red and insert 1 in magenta. The second protomer is in gold. (B) Ribbon representation of Tvpa, with the  $\alpha$ 1 helix colored red, insert 1 magenta, and insert 1' gold. The rest of Tvpa is colored gray. (C) Ribbon representation of hFGE. The disulfide bond between C218 and C365 is represented as sticks. The  $\alpha$ 1 helix is red and insert 1 is magenta. The rest of hFGE is colored gray.



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Mtd-P1 337 AAALFGGANN.GSLS.GSRAALWYSG.PSPSFVFFGARGVCDHL.ILE 381
hFGE   329 ...KKGGSYMCHRSYCYRYRCAARSQNTFDSASNLGFRCAADRLPTMD 371

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**Fig. 54.** Relationship of Mtd to FGE. Superposition of the VR of Mtd-P1 (orange) and the catalytic site of hFGE (green) in  $C\alpha$  representation. *Bottom:* Sequence alignment of the regions shown above. Mtd-P1 variable residues denoted by spheres and hFGE catalytic residues by arrows. Identical residues are in red and chemically similar ones are in blue.

**Table S1. Crystallographic statistics**

Parameter	Native	Hg derivative
Data collection		
Space group	P2 <sub>1</sub> 2 <sub>1</sub> 2 <sub>1</sub>	P2 <sub>1</sub> 2 <sub>1</sub> 2 <sub>1</sub>
Cell dimensions <i>a</i> , <i>b</i> , <i>c</i> , Å	41.39, 77.63, 88.92	41.59, 77.24, 87.37
Wavelength, Å	1.033	0.98792
Resolution, Å*	44.46–1.40 (1.46–1.40)	38.63–2.10 (2.21–2.10)
Completeness, %*	99.9 (100)	99.4 (99.9)
R <sub>merger</sub> , %*	10.7 (31.7)	9.3 (33.8)
I/σI*	3.5 (2.2)	6.3 (2.2)
Redundancy*	7.2 (7.0)	6.6 (6.2)
Refinement		
Resolution, Å	44.46–1.40	
No. of reflections	411,914	
R <sub>work</sub> /R <sub>free</sub> , %	14.6/17.3	
No. of atoms		
Protein	2296	
Ligand/ion	36/3	
Water	256	
B factors, Å <sup>2</sup>		
Protein	13.06	
Ligand/ion	28.02/17.03	
Water	25.28	
rmsd		
Bond lengths, Å	0.0063	
Bond angles, °	1.096	

\*Values in parentheses are for the highest resolution shell.