Literature Report

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Science Contents News Careers Journals

FLUORESCENT PROTEINS

Electrostatic control of photoisomerization pathways in proteins

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June 2000 to present	Camille Dreyfus Distinguished Professor of Chemistry
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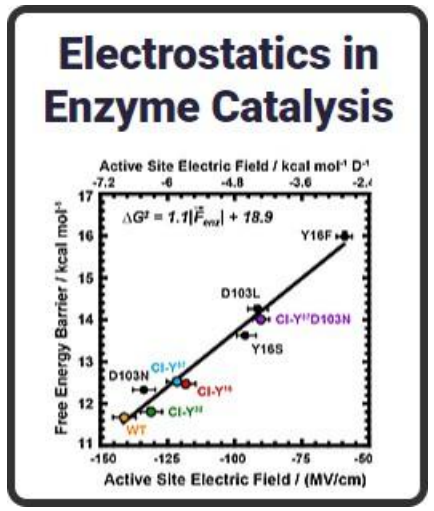
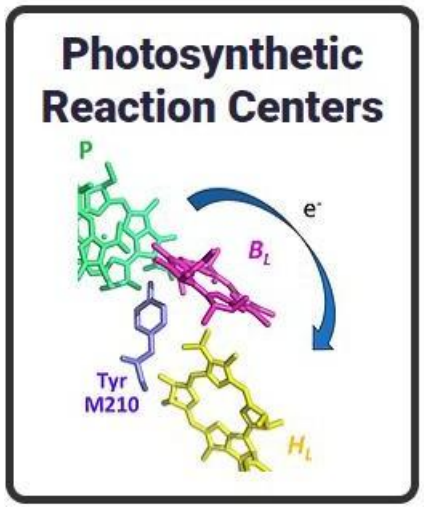
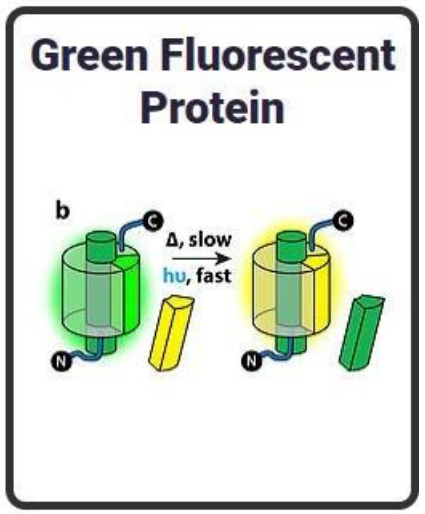
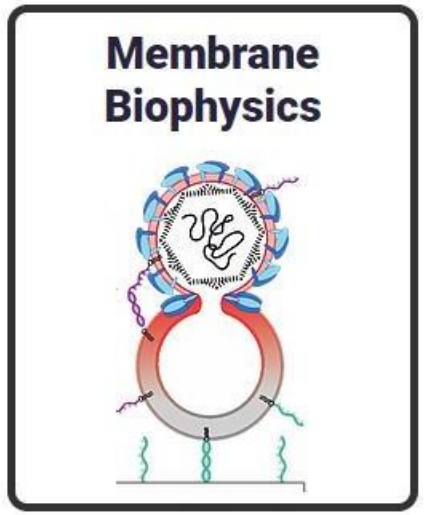
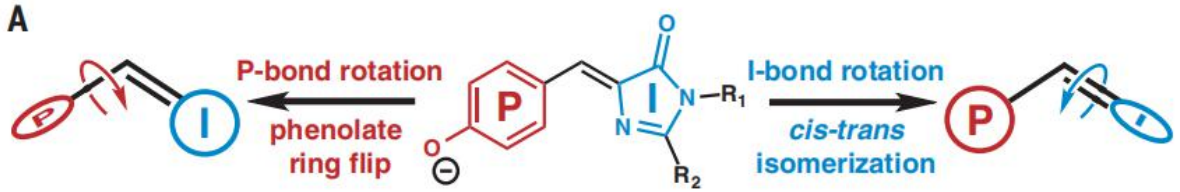
September 1986 to present	Professor of Chemistry, Stanford University
September 1982 to August 1986	Associate Professor of Chemistry, Stanford University
December 1976 to August 1982	Assistant Professor of Chemistry, Stanford University

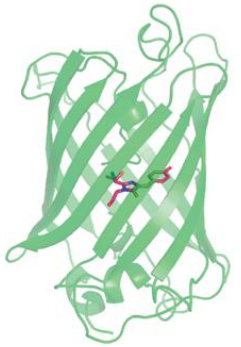






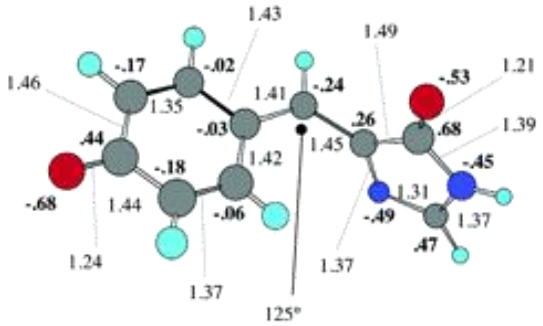






i→p

p→i



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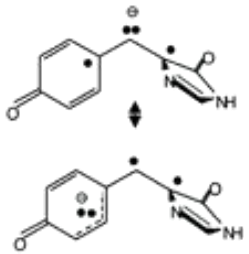
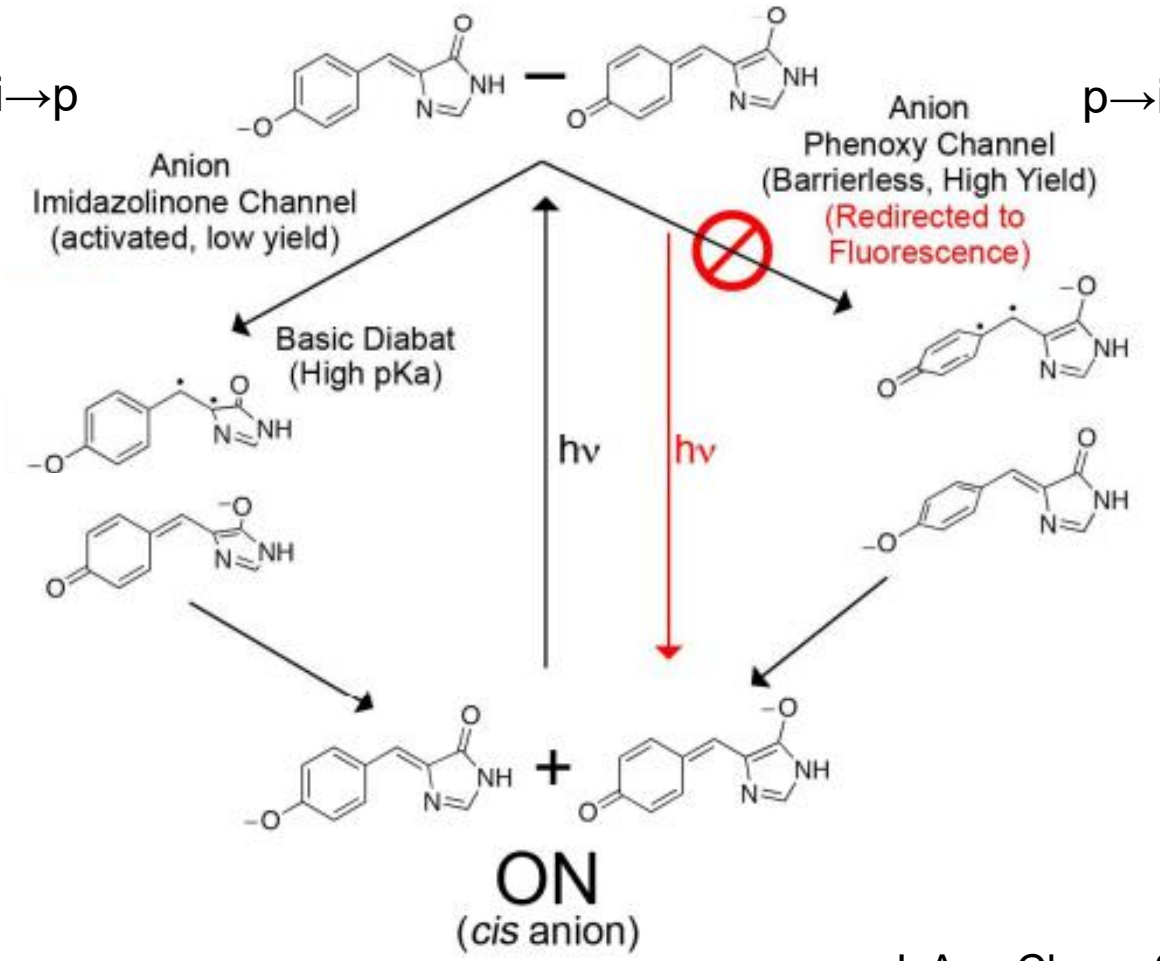
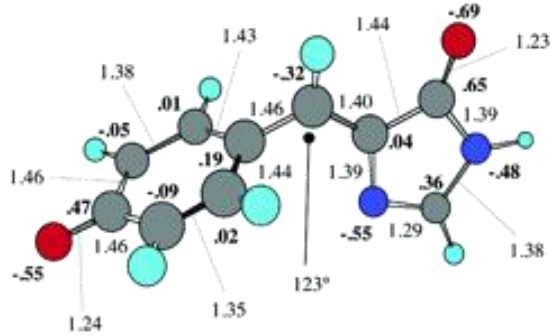
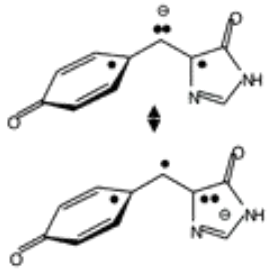


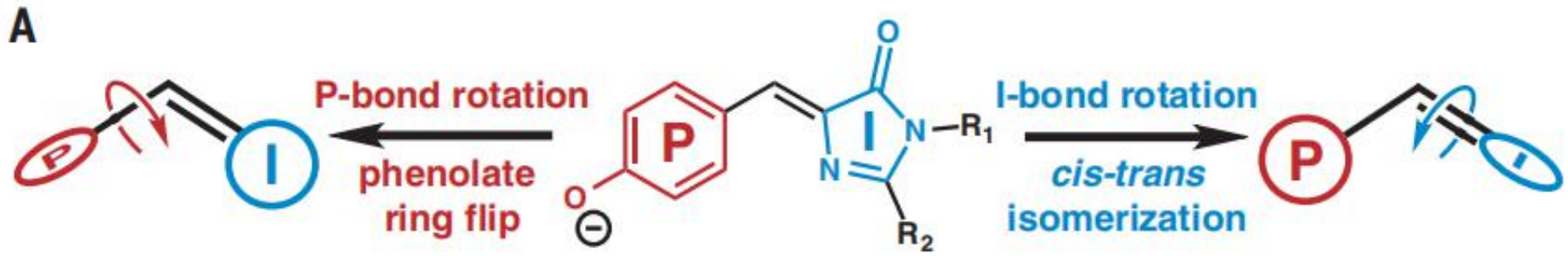




TI1



J. Am. Chem. Soc. 2010, 132, 4, 1192–1193
J. Am. Chem. Soc. 2004, 126, 17, 5452–5464



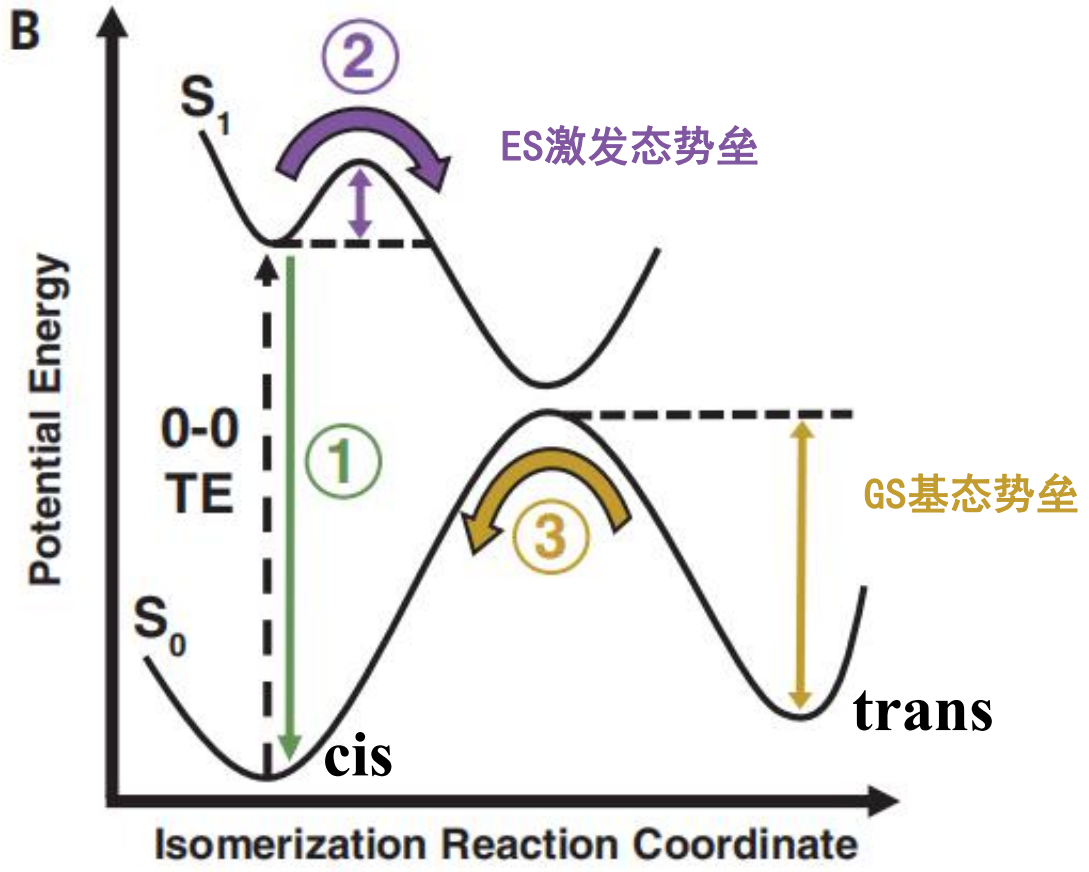
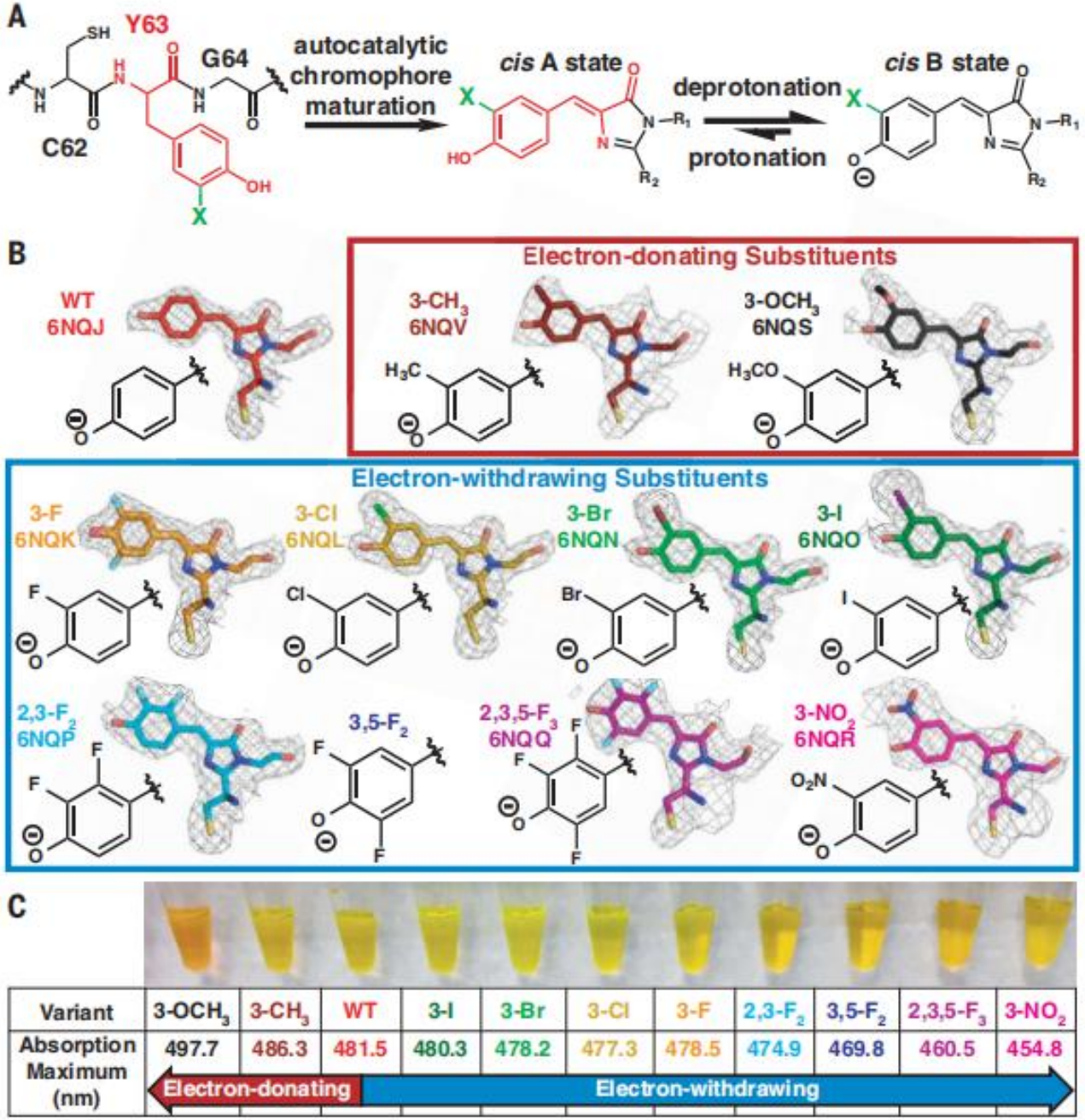
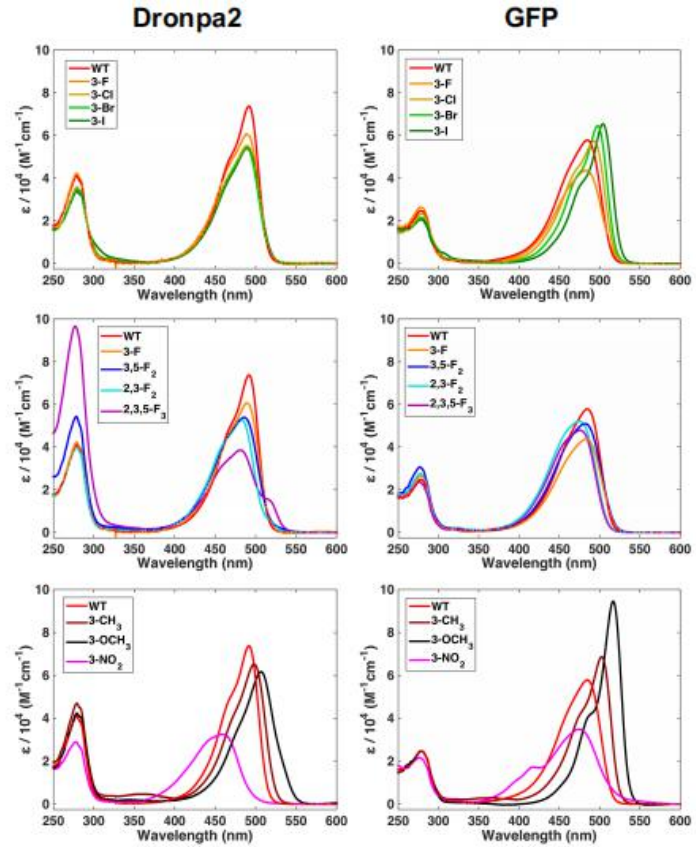
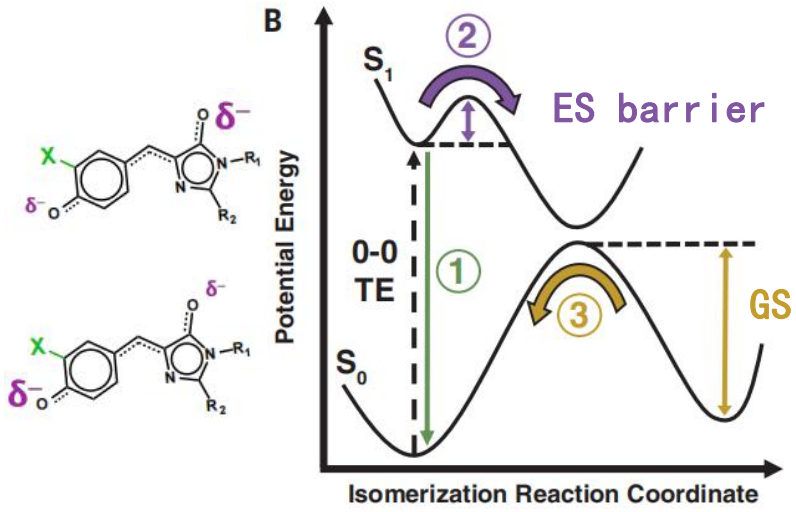


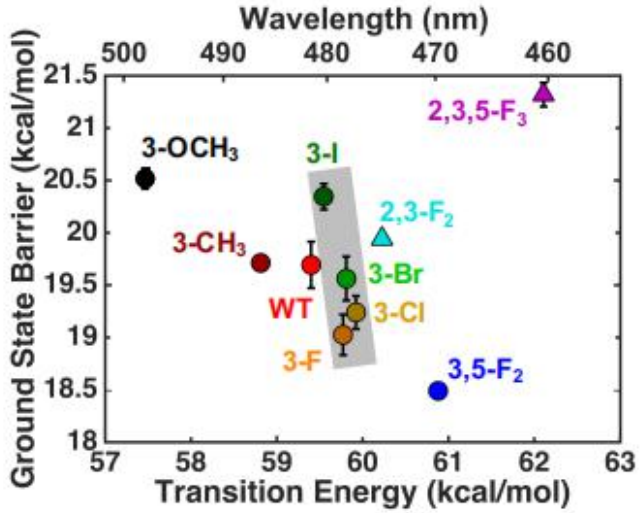
Fig. 1. Model for chromophore isomerization in FPs. (**A**) Rotation can occur about either the P or I bond, leading to a P-ring flip or cis-trans isomerization, respectively. R_1 and R_2 represent residues Gly^{64} and Cys^{62}, respectively, which covalently link the chromophore to the rest of the FP (Fig. 2A). (**B**) General potential energy diagram along the isomerization reaction coordinate for a photoisomerizable chromophore. 0-0 TE represents the TE between the lowest vibrational state of the ground and excited electronic states. Three features studied in this work are emphasized: fluorescence (1, green), ES barrier crossing (2, purple), and GS barrier crossing (3, yellow).

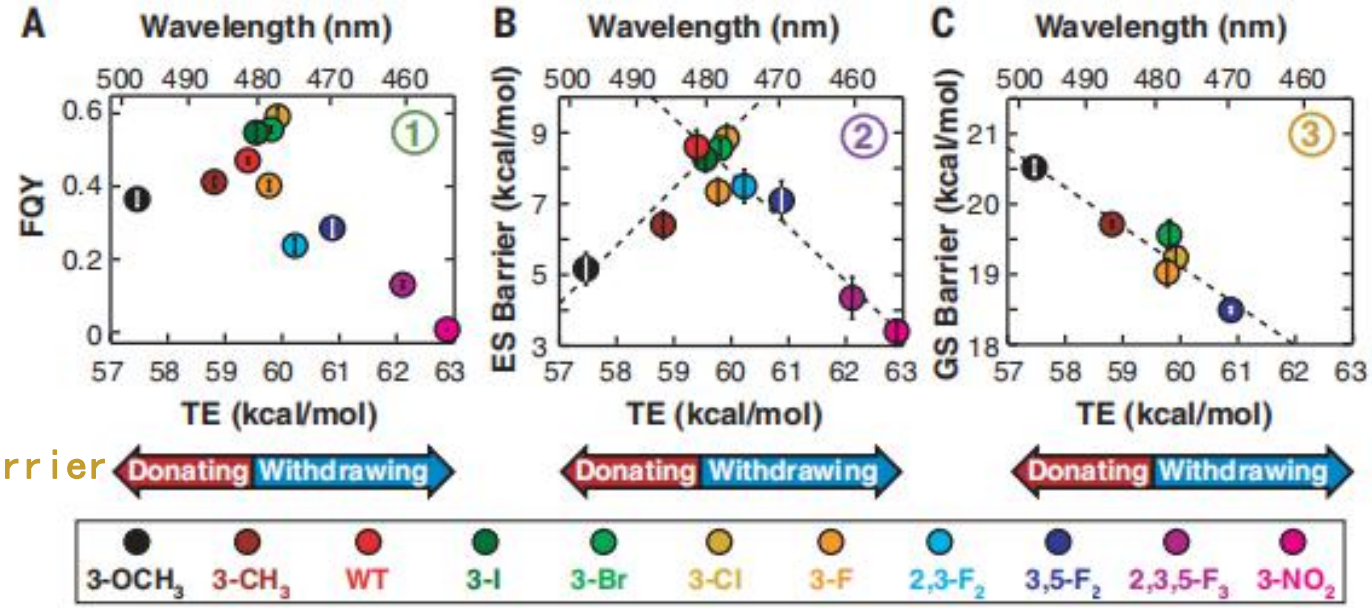

A
Y63
G64
C62
autocatalytic chromophore maturation
cis A state
deprotonation
protonation
cis B state
B
Electron-donating Substituents
WT 6NQJ
3-CH3 6NQV
3-OCH3 6NQS
Electron-withdrawing Substituents
3-F 6NQK
3-Cl 6NQL
3-Br 6NQN
3-I 6NQO
2,3-F2 6NQP
3,5-F2
2,3,5-F3 6NQQ
3-NO2 6NQR
C
Variant | 3-OCH3 | 3-CH3 | WT | 3-I | 3-Br | 3-Cl | 3-F | 2,3-F2 | 3,5-F2 | 2,3,5-F3 | 3-NO2
Absorption Maximum (nm) | 497.7 | 486.3 | 481.5 | 480.3 | 478.2 | 477.3 | 478.5 | 474.9 | 469.8 | 460.5 | 454.8
Electron-donating
Electron-withdrawing


Dronpa2
GFP
WT
3-F
3-Cl
3-Br
3-I
3,5-F2
2,3-F2
2,3,5-F3
3-CH3
3-OCH3
3-NO2
ε / 10^4 (M^-1 cm^-1)
Wavelength (nm)

0-0 跃迁能
（TE）







D Summary of ground and excited state properties of Dronpa2 amber suppression variants

Photophysical Process		Charge Transfer Extent[a]	Electron Flow	Sensitivity to Sterics
Excitation		+1 (by definition)	P ⟶ I	no
ES Barrier Crossing	Withdrawing	-1.5	I ⟶ P	minimal
	Donating	+1.6	P ⟶ I	minimal
GS Barrier Crossing		-0.6	I ⟶ P	yes

[a] Refers to the degree of charge transfer of a given process, determined by the slopes in B and C, compared to that of the excitation process

Fig. 3. GS and ES properties of Dronpa2 amber suppression variants. Circled numbers refer to processes depicted in Fig. 1B. (**A**) FQY versus TE and (**B**) ES energy barrier height versus TE both exhibit a peaked shape (see fig. S7 for comparable FQY results from GFP variants). Linear fits to the electron-donating and electron-withdrawing substituent data in (B) are shown as dashed lines with positive and negative slope, respectively. (**C**) Isosteric series of the GS energy barrier height plotted against TE, with a dashed line representing a linear fit. (**D**) Summary of GS and ES properties of Dronpa2 variants.

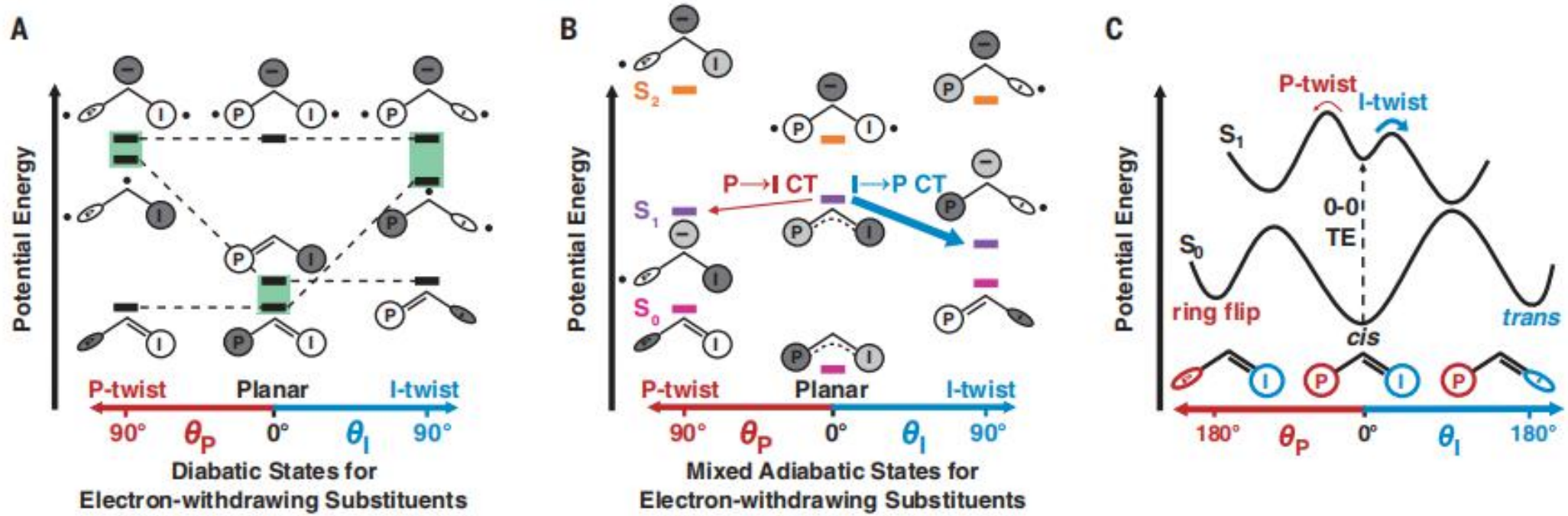


Fig. 4. Allylic anion model of isomerization for a chromophore containing an electron-withdrawing substituent. Shades of gray represent relative magnitude of negative charge localized to the methine bridge, P ring, or I ring, and dots represent unpaired electrons. The color scheme is equivalent to that in Fig. 1A. (**A**) Three diabatic states of the chromophore in planar, I-twisted, and P-twisted geometries, with energetic penalties required for breaking double bonds for rotation. Mixing of the coupled states (highlighted in green) leads to the adiabatic states shown in (**B**). For variants with electron-withdrawing substituents, the I-twist pathway is more energetically downhill, and thus preferred, compared with the P-twist pathway. Electron-donating substituents would have the opposite energetic effect and favor the P-twist pathway (not shown for clarity). Although the relative energy levels of this allylic anion model are qualitative, they are consistent with high-level calculations on the free chromophore at different bond rotation geometries (*15*). Negative charge transfer (CT) occurs from I to P for the I-twist pathway and from P to I for the P-twist pathway, which agrees with a Hammett analysis (supplementary text S3) and simulations of the free chromophore (*5*, *14*). (**C**) Potential energy diagram for FP chromophore isomerization with two competing bond rotation pathways inspired by the mixed adiabatic states in (B). The GS cis chromophore is excited from S_0 to S_1 and relaxes to an S_1 local minimum (relaxation coordinate not shown) (*13*). From the S_1 minimum, the chromophore rotates about either the P or the I bond, depending on the relative ES barrier heights of the competing processes. The diagram represents Dronpa2 variants with electron-withdrawing substituents; variants with electron-donating substituents would have an inverted barrier height ratio between the two competing twisting pathways.

THANKS!