Vitamin K is an important vitamin that mediates, by means of the vitamin K-dependent $\gamma$-glutamyl carboxylase (GGCX) the activation of important blood clotting factors. The vitamin requires rapid recycling in the living organism, and this is accomplished by means of the vitamin K cycle, in which vitamin K (the naphthoquinone form, taken in as part of the diet) is first reduced by the vitamin K epoxide reductase complex 1 (VKORC1) or the NADH-dependent vitamin K quinone reductase (KQR) to the active, (naphthohydroquinone) form. This form of vitamin K then participates in one of the most remarkable transformations in any system. The naphthohydroquinone reacts with molecular oxygen in the presence of a base strong enough to deprotonate the phenol, to give the 2,3-epoxy-1,4-naphthoquinone form (the vitamin K epoxide) of the vitamin, and a species that activates the side chains of glutamate (Glu) residues in the substrate to permit them to react with molecular carbon dioxide to give the corresponding $\gamma$-carboxyglutamate (Gla) residues and a molecule of water.

We are currently involved in computational work to elucidate the details of the mechanism by which the enzyme accomplishes this transformation. If we are successful, this may lead to discovering new compounds that are useful as oral anticoagulants, that also have a rescue mechanism in the case of over-anticoagulation.
In another application of the highly fluorescent aminonaphthalimide fluorophore, we have become involved in the search for fluorescent organic compounds for applications in medicine and histopathology. Again, the 4-alkylamino-1,8-naphthalimide nucleus provides an excellent scaffold on which to construct a variety of site-selective probes for fluorescence microscopy. These dyes are easily delivered to the cell, sequester rapidly, and in a highly selective way in the target organelle. In the absence of intense laser light, are non-toxic, allowing their use in live cells. Importantly, these dyes do not undergo rapid photochemical bleaching under normal epifluorescence illumination. At present, these dyes are available for the observation of lysosomes, mitochondria, Golgi body and its associated transport vesicles, and high-cholesterol or other highly ordered microdomains of membranes.

The compounds themselves are essentially non-toxic, and their large Stokes shift (typically \( \approx 80-100 \) nm) makes them ideal for use in living cells. They have the added advantage that they are excited in the visible range, instead of the ultraviolet, and they are extremely resistant to photochemical bleaching. These properties make them ideal probes for living cells, and we have used this scaffold to build site-specific fluorescent labels for live cells.