Mitochondria-targeted CO-releasing molecule

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I. Introduction
Carbon monoxide (CO) has been recently recognized as a gasotransmitter.1-3 Due to its high affinity for ferrous heme-containing proteins, one of the recognized CO targets is mitochondrial cytochrome c oxidase (CoX). Interaction of CO with CoX has been shown to inhibit cellular metabolism, mito balance, and programmed cell death.4-6 To date, primarily three CORMs have been used as CO donors in studies of mitochondrial function (Figure 1).7 All are metal carbonyl complexes that release CO in a non-physiological, solution-driven manner. These complexes also likely exhibit variability in cell penetration and localization that cannot be assessed by common microscopy methods. To advance studies of the biological effects of CO on mitochondrial function, we designed the first diazaphosphine visible light-driven CO-releasing mitochondria (CORMs) to improve delivery and intracellularly trackable mitochondria-Co-Donor. We hypothesized that structural modification via addition of a TPP tail to the CO-donating core of 1 would enable mitochondria-specific CO release. Such a strategy provides a new chemical tool to study cellular bioenergetics with CO delivered directly at the mitochondria.

II. Synthesis of mitochondria-targeted flavonoids

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III. Absorption/emission in cell culture medium with 10%FBS

IV. Photoinduced CO-release reactivity of new analogs

V. Confocal imaging of mitochondrial localization

VI. Co-localization and intensity profile

VII. Intracellular photodegradation

VIII. Cytotoxicity studies on CO released in situ

IX. The effects of CO on mitochondrial bioenergetics

X. CORMs and mitochondrial bioenergetics, overview

XI. Summary

In the work described herein, we have presented the first example of CO donor targeted to mitochondria. This CORM has the following features:

* Triggerable: delivered directly to mitochondria
* Effective: Induces bioenergetics response at as low as 1 μM

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References