Atomic Vacancy Rich Molybdenum Disulfide Nanoparticles Stimulate Mitochondrial Biogenesis and Enhance Oxidative Phosphorylation

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Reduced mitochondrial function is the basis of many rare congenital diseases of energy metabolism and contributes to most common age-associated metabolic and neurodegenerative disorders. Therefore, boosting mitochondrial biogenesis is an intriguing therapeutic approach for these diseases; however, currently there exists a limited repertoire of compounds that can stimulate mitochondrial function. To address this, we designed molybdenum disulfide (MoS_2) nanoflowers with predefined atomic vacancies that are fabricated by self-assembly of individual two-dimensional MoS_2 nanosheets. The treatment of mammalian cells with MoS_2 nanoflowers increased mitochondrial biogenesis by induction of PGC-1α and TFAM, which resulted in increased mitochondrial DNA copy number, enhanced expression of nuclear and mitochondrial-DNA encoded genes, and increased levels of mitochondrial respiratory chain proteins. Consistent with increased mitochondrial biogenesis, treatment with MoS_2 nanoflowers enhanced mitochondrial respiratory capacity and adenosine triphosphate production in multiple mammalian cell types. Taken together, this study reveals that predefined atomic vacancies in MoS_2 nanoflowers stimulate mitochondrial function by upregulating the expression of genes required for mitochondrial biogenesis.

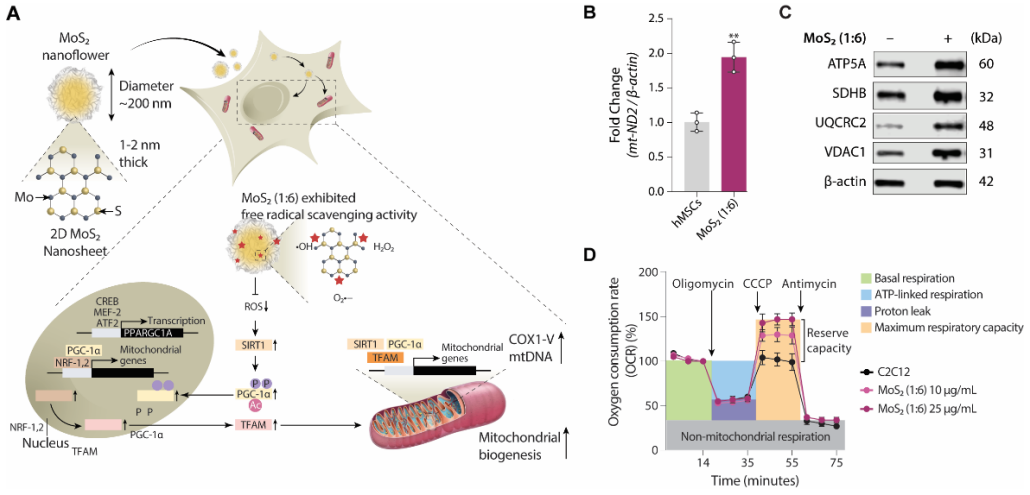

Figure 1: (A) Proposed mechanism of action by which vacancy rich MoS_2 (MoS_2 (1:6)) enhance mitochondrial biogenesis. **(B)** A significant increase in mt-DNA encoded transcript (*mt-ND2*), was observed in cells following MoS_2 treatment, indicating increased mitochondrial biogenesis. **(C)** Western blotting is used to determine the relative expression of key mitochondrial proteins, with MoS_2 (1:6) treatment resulting in a significant upregulation these proteins. **(D)** The effect of MoS_2 on oxygen consumption rate (OCR) was determined in C2C12 cells treated with different concentrations of MoS_2 (1:6) (0, 10 and 25 µg/mL). Treated cells exhibited an increase in the maximum respiratory capacity.

References:

Singh, Kanwar Abhay, et al. "Atomic vacancies of molybdenum disulfide nanoparticles stimulate mitochondrial biogenesis." *Nature Communications* 15.1 (2024): 8136.