An essential role for NAD(P)H oxidase 2 in UVA-induced calcium oscillations in mast cells

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UVA can penetrate to skin dermis, to be absorbed by endogenous photosensitizers in dermal fibroblasts, granular leukocytes, endothelial cells and mast cells. Solar UVA radiation (320-340 nm) is known to have immunemodulatory effects, but the detailed mechanisms involved are not fully elucidated.

UVA irradiation has been shown to induce calcium oscillations in rat peritoneal mast cells due to NAD(P)H oxidase (NOX) activation, but the specific NOX isoforms have not been identified. In the present work effects of UVA irradiation were investigated in isolated rat peritoneal mast cells, in cultured rat mast cell line RBL-2H3, and in mouse bone marrow-derived mast cells (BMMC). It was found that UVA irradiation by alternate 340/380 nm (3.2-5.6 μ W.cm-2) or by LED (380 nm, 80 μ W.cm-2) induced calcium oscillations in isolated rat peritoneal mast cells, in RBL-2H3, and in BMMC. It was found that RBL-2H3 expressed high level gp91phox (NOX2), p22phox, p67phox, p47phox, p40phox and Rac 1/2 were confirmed by immunocytochemistry. UVA-induced reactive oxygen species (ROS) production in RBL-2H3 was completely suppressed by NOX inhibitor diphenyleneiodonium (DPI) or by antioxidant N-acety-L-cysteine (NAC). siRNA suppression of gp91phox (NOX2), p22phox, p47phox expression inhibited markedly UVA-induced calcium oscillations, ROS and IL-6/ LTC4 production in RBL-2H3.

Taken together these data indicate that NOX2 plays an essential role in UVA irradiation–induced calcium oscillations, ROS and mediator production in all three types of mast cells. The present findings may open up new avenues for NOX2-focused treatment of solar irradiation-induced skin conditions.

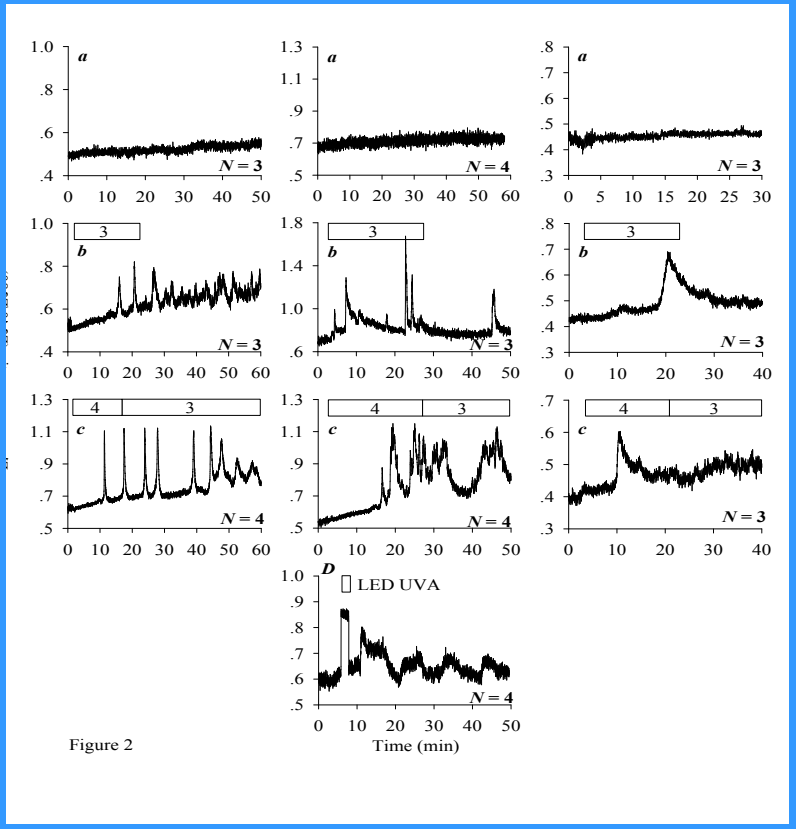

Figure 2

Figure 2. UVA irradiation induced calcium oscillations in mast cells.Fura-2-loaded rat peritoneal mast cells (A), cultured RBL-2H3 (B, D), or mouse BMMC (C) were perifused, the monochromater slit-width was increased from 2 to 3 or 4 nm as indicated by the horizontal bars (A-C), or slit width was maintained at 2nm but irradiated with an LED source (D). Calcium tracings in each panel (obtainedfrom one individual cell in the PMT-based system) are representative of N (asindicated) independent experiments. UVA power for monochromater (alternating340/380 nm) slit width 2, 3, 4 nm were 1.5, 3.2, 5.6 μ μ .cm-2 respectively. LED powerwas (380 nm, 80 μ μ .cm-2).