Supplemental Text – Materials and Methods:

Purification of pdg enzymes: After the appropriate pET-22b (+) vector for expression of pdgs was transformed into *Escherichia coli* BL21 (DE3-RILP) (Agilent Technologies, Cedar Creek, TX), bacteria were grown to an OD_{600} of 0.6 in 1.5 L of LB media and protein expression was induced with the addition of IPTG to a final concentration of 0.5 mM for 8 hours at 18°C. Cells were harvested by centrifugation at 4000 x g for 20 minutes. The cell pellet was resuspended in 40 ml of buffer 1 [50 mM sodium phosphate (pH 7.0), 300 mM NaCl, and 10 mM imidazole with EDTA-free protease inhibitors (Roche Diagnostics, Indianapolis, IN)] and lysed by passage through a French pressure cell at 10,000 psi. Cell debris was removed by centrifugation at 10,000 x g for 20 minutes. The supernatant was added to 10 ml of Ni-NTA agarose beads (Qiagen, Valencia, CA) and proteins were batch bound for 20 minutes at 4°C followed by centrifugation at 700 x g for 4 minutes. The matrix was washed 4 times for 20 minutes each at 4°C [twice in buffer 1 and twice in buffer 2 (50 mM sodium phosphate (pH 7.0), 300 mM NaCl, and 50 mM imidazole with EDTA-free protease inhibitors)], then loaded onto a column, allowed to settle via gravity, and washed with 4 column volumes of buffer 2 until no residual 280 nm absorbing materials were eluted. The matrix-bound pdgs were eluted with 50 mM sodium phosphate (pH 7.0), 300 mM NaCl, and 400 mM imidazole with EDTA-free protease inhibitors at a flow rate of 2 ml/minute. Protein purity was evaluated by electrophoresis through a 15% SDS-PAGE gel followed by Coomassie blue staining. Due to the observation that the pdg proteins adhere to plastic surfaces, all tubes and plates used throughout these experiments were siliconized with Sigmacote (Sigma-Aldrich, Saint Louis, MO) followed by desiccation in air.

Preparation of cell lysates and concentrated medium: HaCaT keratinocytes and immortalized human fibroblasts were incubated with Cv-pdg-NLS-TAT in the medium prior to being harvested by scraping into PBS and concentrated by centrifugation at 175 x g for 5 minutes. To generate whole cell lysates, cell pellets were resuspended in 10 mM Tris-HCl (pH 7.8), 200 mM KCl, followed by addition of an equal volume of 10 mM Tris-HCl (pH 7.8), 200 mM KCl, 2 mM EDTA (pH 8.0), 2 mM DTT, 0.2% NP-40, 40% glycerol, and supplemented with complete protease inhibitors (Roche Diagnostics). After incubation for 1 hour with rocking at 4°C, the cells were collected by centrifugation at 16,000 x g for 10 minutes and the supernatant retained. To generate cytoplasmic and nuclear fractions, cell pellets were resuspended in 10 mM Hepes (pH 7.9), 1.5 mM $MgCl_2$, 10 mM KCl, 0.5 mM DTT and EDTA-free complete protease inhibitors. Cells were allowed to swell on ice for 15 minutes before 1/10 volume of 10% NP-40 was added to the cell suspension. The samples were incubated with rocking at 4°C for 30 minutes and pelleted at 16,000 x g for 10 minutes. The cytoplasmic supernatant was removed from the pellet and RIPA buffer [final concentration 50 mM Tris-HCl (pH 7.5), 150 mM NaCl, 1% NP-40, 0.5% deoxycholate, and EDTA-free complete protease inhibitors] was added. The remaining nuclear pellet was resuspended in 250 mM sucrose, 10 mM $MgCl_{2,}$ and EDTA-free protease inhibitors and layered over an equal volume of 350 mM sucrose, 10 mM $MgCl_{2,}$ and EDTA-free protease inhibitors, followed by centrifugation at 1450 x g for 5 minutes. This pellet was resuspended in 350 mM sucrose, 10 mM $MgCl_{2,}$ and EDTA-free protease inhibitors and sonicated in 8 x 10 second bursts at 6X power in a circulating ice water bath in a Misonix 3000 cuphorn sonicator (Misonix, Inc, Farmingdale, NY). The sample was

then layered over an equal volume of 880 mM sucrose, 10 mM $MgCl_2$, and EDTA-free protease inhibitors and spun at 16,000 x g for 10 minutes to pellet any remaining insoluble material. The nuclear supernatant was adjusted with RIPA buffer to a final concentration as described above. To concentrate the keratinocyte medium, 5 ml medium from each 100 mm plate were collected at 3200 x g for 22 minutes at 4^oC in a 15 ml centrifugal filter device. The final volume was approximately 1 ml after concentration.

Immunoblots: Protein concentrations were determined by spectrophotometry readings at 595 nm compared to bovine serum albumin (BSA) standards (New England BioLabs, Ipswitch, MA) using Bradford protein dye reagent (Bio-Rad, Hercules, CA). A total of 20 μg of cellular lysate (or 300 μg of concentrated medium) was incubated for 5 minutes at 95^oC in sample buffer [final concentration of 50 mM Tris-HCl (pH 6.8), 100 mM DTT, 2% SDS, 10% glycerol, and 0.1% bromophenol blue] and separated by 15% SDS-PAGE in electrophoresis buffer (25 mM Tris-HCl, 192 mM glycine, and 0.1% SDS). Proteins were transferred to nitrocellulose membranes (Whatman, Dassel, Germany) in 4^oC transfer buffer (electrophoresis buffer with 20% (v/v) methanol added) at 100 volts for 1 hour. Membranes were blocked in TBS-t [50 mM Tris-HCl (pH 7.5), 200 mM NaCl, 0.05% Tween-20] containing 10% (w/v) nonfat milk powder for 1 hour at RT, followed by overnight incubation at 4^oC with specific antibodies to Cv-pdg (produced in rabbits against the full length non-denatured protein), α-tubulin (Sigma-Aldrich), or histone H3 (Active Motif, Carlsbad, CA). Membranes were incubated for 1 hour at RT in TBS-t containing 5% milk with secondary IgG-HRP antibodies, washed three times (20 minutes each) with TBS-t 5% milk, rinsed in TBS-t, and incubated for 5 minutes in Western Lightning Chemiluminescence Reagent Plus (Perkin-Elmer, Waltham, MA). Proteins were visualized by exposure to Kodak film.

Preparation of human skin model for histology, IIF, or immunoblot: Upon harvest of the Epi-derm FT™ samples (Mattek, Ashland, MA), tissues were cut and either frozen in liquid nitrogen for protein extraction, fixed in 10% neutral buffered formalin that contains 4% formaldehyde (Sigma-Aldrich) for H&E staining and IIF, or fixed in 75% MeOH: 25% acetic acid for 20 minutes, followed by placing in 70% EtOH until processing for detection of CPDs (as described in (Schul, Jans et al. 2002). Tissues were embedded in paraffin blocks, cut into 5 μm sections, and H&E staining performed by the OHSU Knight Cancer Institute Histology Core. For IIF microscopy, the slides were processed through standard washes in xylenes and EtOH dilutions. Protein epitopes were retrieved by immersion in boiling citrate buffer (pH 6.0), followed by cooling to RT (this step was not included for analysis of CPDs). Primary antibodies [anti-cytokeratin 14 (Fitzgerald, Concord, MA), anti-loricrin (Covance, Emeryville, CA), anti-Cv-pdg, or anti-CPD (Cosmo Bio Co., LTD, Tokyo, Japan)] were incubated at 4^oC overnight and secondary antibodies [Alexa Fluor 594-conjugated goat anti-guinea pig, Alexa Fluor 488- or 594-conjugated goat anti-rabbit, or Alexa Fluor 594-conjugated goat anti-mouse (Invitrogen)] were incubated for 30 minutes at RT in darkness in PBS with 12% BSA, followed by PBS washes. Cover slips were mounted using ProLong Gold Antifade Reagent with DAPI (Invitrogen) applied to the tissues. To prepare protein lysates, the tissues that had been frozen in liquid nitrogen were pulverized using a mortar and pestle, resuspended in 2X sample buffer (see immunoblot methods), and boiled for 10 minutes.

IIF microscopy for CPDs: HaCaT keratinocytes and immortalized human fibroblasts were seeded onto microscope cover slips in a 6-well tissue culture dish and grown to ~ 60% confluence. Either buffer or the Cv-pdg-NLS-TAT protein was delivered to the medium and cells were incubated for 4 hours prior to being exposed to 100 J/m^2 UVB. At the indicated times following UVB exposure, the cells were fixed in 75% methanol: 25% acetic acid for detection of CPDs. The CPD detection protocol was as described in (Schul, Jans et al. 2002). Cells were incubated overnight at 4°C with CPD antibody diluted in blocking buffer, then washed and incubated with an Alexa Fluor 488-conjugated secondary goat anti-mouse IgG in the dark. Each microscope cover slip was washed and mounted onto a microscope slide using ProLong Gold antifade reagent with DAPI. Cells were visualized for CPD IIF intensity with a Zeiss Axioskop 2 microscope at 40X magnification. Comparative pictures were taken at the same exposures and processed equally.

Supplemental Reference for Materials and Methods:

Schul, W., J. Jans, et al. (2002). "Enhanced repair of cyclobutane pyrimidine dimers and improved UV resistance in photolyase transgenic mice." Embo J **21**(17): 4719-29.