[0021] **FIGS. 12A-12B:** The F623 and M639 mutations cannot separate activity of MF and DEX. FIG. 12A shows transactivation activity of F623 mutations on MMTV-Luc in AD293 cells. DEX 10 nM, MF 1 nM. Error bars stand for standard deviation, n = 3. FIG. 12B shows transactivation activity of M639 mutations on MMTV-Luc in AD293 cells. DEX 10 nM, MF 1 nM. Error bars stand for standard deviation, n = 3.

[0022] **FIGS. 13A-13B:** *In vitro* binding assay of GR Q642A mutant protein. (FIG. 13A) *in vitro* ligand binding experiment using cytosol from AD293 cells that expressed either wild type GR or Q642A mutant GR. CPM: counts per minute. Error bars stand for standard deviation, n = 2. (FIG. 13B) DEX dose response curve of WT GR and Q642A GR in a MMTV-Luc reporter assay. Error bars stand for standard deviation, n = 3. (C), GR Q642A ligand competition assay. Error bars stand for standard deviation, n = 2.

[0023] **FIG. 14:** Activity bar graph of the compounds of the invention, provided as Relative Luciferase Units.

[0024] **FIG. 15:** Line graph showing the 8-fold increase in potency of Compound 4 over fluticasone furoate (FF).

[0025] **FIGS. 16A-16B:** (FIG. 16A) A line graph providing the potency of candidate compounds in a reporter system. (FIG. 16B) A line graph providing the evaluation of the effect of candidate compounds in repressing lung inflammation, using a OVA-induced mouse asthma model.

[0026] The foregoing figures are provided for exemplary purposes, and are not meant to be limiting in any way.

DETAILED DESCRIPTION

[0027] Glucocorticoids have been in use for almost 60 years and they remain the first choice for treating many inflammatory and autoimmune diseases. However, long-term use of glucocorticoids can cause many adverse effects. Understanding the structural basis of GR activation and repression is very important for developing novel glucocorticoids with less side effects. However, the low expression level of GR in bacterial system, especially for low affinity ligand, hampered the structural study of this important cellular regulator. Via comparing conserved residues in steroid receptor family, the inventors had successfully identified amino acid mutations that could facilitate receptor expression without affecting receptor physiology function. This method will accelerate the structural study of GR, especially for those low affinity ligands, such as non-steroid ligand, which may hold the future of next generation glucocorticoid.

[0028] The development of highly potent glucocorticoids was propelled by two types of urgencies, one is the side effects of glucocorticoids caused by high dose usage, and the other