Inducible Homodimerization Citations

Clontech’s iDimerize™ Inducible Homodimer System was previously available from ARIAD as the ARGENT Regulated Homodimerization Kit and AP20187 ligand.

Fusion proteins containing the DmrB domain do not interact until the B/B Homodimerizer is added. This cell-permeable ligand induces the fusion proteins to interact, activating downstream signaling in real time. This example shows activation of a signal transduction pathway through dimerization of a membrane-bound receptor domain.
indicating a potential role of caspase activation downstream of NLR activation in Hydra.

The authors show induced proximity recruitment of an effector caspase (HyDD-Caspase) to the HyNLR type 1 protein upon oligomerization, but not LC3 binding. Self-oligomerization of p62 is essential for its localization to the autophagosome formation site.

ΔEGFR is a potent oncogene despite, not because of, its low intensity. implying that the ΔEGFR does not form strong or stable dimers as part of its low level signal. Forced dimerization enhanced the oncogenic signal of the receptor, ΔAP20187-induced dimerization of chimeric oligosaccharide destruction, suggesting a novel mammalian stress-signaling pathway.

mediated dimerization of the IRE1 alpha cytosolic unit activated glycogenolysis, releasing mannose-6-phosphate and causing lipid-linked mannose-6-phosphate regulates destruction of lipid-linked oligosaccharides. AP20187-mediated oligomerization of MDM2 partially overcame the inhibitory effect of ATM-mediated phosphorylation of the upstream sequence pathways as endogenous FGFR1 and led to an increase in cellular migration, proliferation and signaling.

of alternatively activated m2 macrophages. The degree and type of inflammatory response upon ablation of live adipocytes have been studied through AP20187-mediated activation of Caspase-8 in a FAT-ATTAC mouse model.

of the epidermal growth factor receptor. Dimerization and activation of iFGFR1 by AP20187 (the B/B Homodimerizer) activated the same signaling pathways as endogenous FGFR1 and led to an increase in cellular migration, proliferation and signaling.

PERK integrates autophagy and oxidative stress responses to promote survival during ECM detachment. Inducible activation of an Fv2E-aNPERR chimera resulted in lumen-filled mammary epithelial acini.

Mammary tumorigenesis induced by fibroblast growth factor receptor 1 requires activation of the epidermal growth factor receptor. Dimerization and activation of FGFR1 by AP20187 (the B/B Homodimerizer) activated the same signaling pathways as endogenous FGFR1 and led to an increase in cellular migration, proliferation and signaling.

Regulation of MDM2 E3 ligase activity by phosphorylation after DNA damage. AP20187-induced oligomerization of MDM2 partially overcame the inhibitory effect of ATM-mediated phosphorylation of the upstream sequence and stimulated p53 ubiquitination.

The degree and type of inflammatory response upon ablation of live adipocytes have been studied through AP20187-mediated activation of Caspase-8 in a FAT-ATTAC mouse model.

Directed depletion of adipocytes by apoptosis leads to adipose tissue recruitment of alternatively activated m2 macrophages. The degree and type of inflammatory response upon ablation of live adipocytes have been studied through AP20187-mediated activation of Caspase-8 in a FAT-ATTAC mouse model.

Activity of the Ste20-like kinase, SLK, is enhanced by homodimerization. Homodimerization of an SLK fusion protein increased the activation-specific phosphorylation of proapoptotic kinases and enhanced apoptosis.

The RapGAP activity of plexins was activated by AP20187-induced dimerization; defining a pathway for plexin signaling and providing insights into the mechanism for semaphorin-induced activation of plexins that could be exploited in regenerative therapies for axon-severing injuries.

Cone degeneration following rod ablation in a reversible model of retinal degeneration. Transgenic X. laevis expressing the Escherichia coli enzyme nitroreductase (NTR) under the control of the rod-specific rhodopsin (XOP) promoter were used to determine the effects of metronidazole on the vision and retinas of XOPNTR F1 tadpoles.

Bone marrow CD169+ macrophages promote the retention of hematopoietic stem and progenitor cells in the mesenchymal stem cell niche. AP20187-treated MaFIA mice were used to study HSC/progenitor maintenance during homeostasis.

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Mannose-6-phosphate regulates destruction of lipid-linked oligosaccharides. AP20187-mediated dimerization of the IRE1 alpha cytosolic unit activated glycogenolysis, releasing mannose-6-phosphate and causing lipid-linked oligosaccharide destruction, suggesting a novel mammalian stress-signaling pathway.

Targeted deletion of adipocytes by apoptosis leads to adipose tissue recruitment of alternatively activated m2 macrophages. The degree and type of inflammatory response upon ablation of live adipocytes have been studied through AP20187-mediated activation of Caspase-8 in a FAT-ATTAC mouse model.

The RapGAP activity of plexins was activated by AP20187-induced dimerization; defining a pathway for plexin signaling and providing insights into the mechanism for semaphorin-induced activation of plexins that could be exploited in regenerative therapies for axon-severing injuries.

Macrophages are crucial for epithelial cell death and adipocyte repopulation during mammary gland involution. The MaFIA mouse model was used to delete macrophages expressing colony stimulating factor 1 receptor during weaning-induced mammary gland involution.

Regulation of MDM2 E3 ligase activity by phosphorylation after DNA damage. AP20187-induced oligomerization of MDM2 partially overcame the inhibitory effect of ATM-mediated phosphorylation of the upstream sequence and stimulated p53 ubiquitination.

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Bone marrow CD169+ macrophages promote the retention of hematopoietic stem and progenitor cells in the mesenchymal stem cell niche. AP20187-treated MaFIA mice were used to study HSC/progenitor maintenance during homeostasis.
2011 Citations…continued

Luhovy, A.Y. et al. (2011) J. Biol. Chem. [Epub ahead of print]. Regulation of the STE20-like kinase, SLK: Involvement of activation segment phosphorylation. To test whether homodimerization of SLK affects phosphorylation, Fv-SLK 1–373 WT was treated with AP20187 to induce regulated dimerization.

Matsui, T. et al. (2011) Proc. Natl. Acad. Sci. USA 108(24):9881–9886. Canopy1, a positive feedback regulator of FGF signaling, controls progenitor cell clustering during Kupffer’s vesicle organogenesis. AP20187-mediated conditional activation of FGFR1 in dorsal forerunner cells of zebrafish led to a 67% reduction in the broken-up dorsal forerunner cells phenotype relative to vehicle (ethanol)-treated controls, suggesting a regulatory mechanism underlying cell cluster formation, which is an indispensable step for formation of a functional Kupffer’s vesicle and establishment of the left–right asymmetric body plan.


Okazuka, K. et al. (2011) Mol. Ther. 19(7):1287–1294. Long-term regulation of genetically modified primary hematopoietic cells in dogs. Nine years ago, two dogs were transplanted with autologous marrow CD34(+) cells encoding a conditionally activatable derivative of the thrombopoietin receptor. Receptor activation through administration of a chemical inducer of dimerization (CID) (AP20187 or AP1903) conferred a growth advantage.

Ouda, R. et al. (2011) J. Biol. Chem. 286(29–12610–12619. Retinoic acid-inducible gene I-inducible miR-23b inhibits infections by minor group rhinoviruses through down-regulation of the very low density lipoprotein receptor. AP20187-mediated oligomerization of the CARD of RIG-I resulted in signaling, activating the IFN-beta and IL-6 genes.


Suzuki, M. et al. (2011) J. Biol. Chem. 286(34):29964–29972. Attenuated CagA oncoprotein in Helicobacter pylori from Amerindians in Peruvian Amazon. Strains of H. pylori from Amerindians from the remote Peruvian Amazon contain novel alleles of cagA, a major virulence gene, and reveal distinctive properties of their encoded CagA proteins. The Amerindian CagA proteins behave as dominant negative inhibitors of prototype CagA during mixed infection of Mongolian gerbils, but the inhibitory effect is avoided when CagA is forcibly premultimerized using AP20187.

Tseng, H-C. et al. (2011) Anticancer Res. 31(12):4239–4249. Cytoskeleton network and cellular migration modulated by nuclear-localized receptor tyrosine kinase ROR1. Activation of FKBP-fused ROR1 with AP20187 led to a significant increase in actin stress fibers and increased cellular migration.


2010 Citations


Dixon, J. E. et al. (2010) Development 137(18):2973–2980. Axolotl Nanog activity in mouse embryonic stem cells demonstrates that ground state pluripotency is conserved from urodele amphibians to mammals. AxNanog dimers are required to rescue LIF-independent self-renewal and promote proliferation.

Hofman, E. G. et al. (2010) J. Biol. Chem. 285(50):39481–39489. Ligand-induced EGF receptor oligomerization is kinase-dependent and enhances internalization. EGF receptor (EGFR) oligomerization was controlled using AP20187 to enhance EGF-induced receptor internalization, and monitored using FRET.
**2010 Citations—continued**

Jiang, Z. et al. (2010). J. Neurosci. 30(7):2582–2594. **eIF2α Phosphorylation-dependent translation in CA1 pyramidal cells impairs hippocampal memory consolidation without affecting general translation.** Conditional transgenic mice were treated with AP20187 to increase PKR-mediated phosphorylation of eIF2 alpha in hippocampal CA1 pyramidal cells, which led to impaired hippocampal late phase-LTP and memory consolidation, but no obvious reduction in general translation.

Karulf, M. et al. (2010). J. Immunol. 185(8):4866–4872. **OX40 ligand regulates inflammation and mortality in the innate immune response to sepsis.** MaFIA mice were used to determine the role of OX40-OX40 ligand (OX40L) interaction in the innate immune response to polymicrobial sepsis.

Krishnamurthy, S. et al. (2010). Cancer Res. 70(23):9969–9978. **Endothelial cell-initiated signaling promotes the survival and self-renewal of cancer stem cells.** AP20187 was used to selectively ablate tumor-associated endothelial cells in xenograft tumors, via a caspase-based artificial death switch (iCaspase-9).

Kuenzel, S. et al. (2010). J. Immunol. 184(4):1990–1999. **The nucleotide-binding oligomerization domain-like receptor NLRC5 is involved in IFN-dependent antiviral immune responses.** AP20187 was used to trigger dimerization and test the role of NLRC5 in the activation of signaling pathways that use the IFN-specific response element and IFN-gamma activation sequence.


Léveillé, F. et al. (2010). J. Neurosci. 30(7):2623–2635. **Suppression of the intrinsic apoptosis pathway by synaptic activity.** Inducible caspase-9 and AP20187 were used to cause cell death in cortical neurons, indicating that pathways downstream of caspase-9 activation are not a significant aspect of the anti-apoptotic effects of synaptic activity.


Oberst, A. et al. (2010). J. Biol. Chem. 285(22):16632–16642. **Inducible dimerization and inducible cleavage reveal a requirement for both processes in caspase-8 activation.** Unlike the executioner caspases, both dimerization and cleavage of caspase-8 are required to activate caspase-8 in vitro and apoptosis in cellular systems.

Pan, P.Y. et al. (2010). Cancer Res. 70(1):99–108. **Immune stimulatory receptor CD40 is required for T-cell suppression and T regulatory cell activation mediated by myeloid-derived suppressor cells in cancer.** MaFIA transgenic mice were implanted intrahepatically with OVA-B16 tumor cells and treated with AP20187 to induce CD115-specific depletion. The results suggest that CD40 is essential for myeloid-derived suppressor cell-mediated immune suppression and for tumor-specific T-regulatory cell expansion.


Priceman, S. J. et al. (2010). Blood 115(7):1461–1471. **Targeting distinct tumor-infiltrating myeloid cells by inhibiting CSF-1 receptor: combating tumor evasion of antiangiogenic therapy.** The MaFIA transgenic mouse model was used to study the impact of macrophage ablation on tumor angiogenesis.


Stuffers, S. et al. (2010). J. Histochem. Cytochem. 58(11):1025–1032. **Time-resolved ultrastructural detection of phosphatidylinositol 3-phosphate.** A monomeric dimerizable FYVE probe and rapalog-induced dimerization were used to follow the distribution of phosphatidylinositol 3-phosphate (PtdIns(3)P) at the ultrastructural level.


2010 Citations…continued


Zhao, L. et al. (2010) J. Biol. Chem. 285(4):2488–2497. Dimerization of CPAP orchestrates centrosome cohesion plasticity. HeLa cells expressing tFLAG-CPAP-FKBP were treated with AP20187 to study the role of CPAP dimerization in centrosome maintenance and cohesion, and in accurate cell division.

2009 Citations


Chinnery, H. R. et al. (2009) J. Immunol. 182(5):2738–2744. Bone marrow chimeras and c-fms conditional ablation (MaFIA) mice reveal an essential role for resident myeloid cells in lipopolysaccharide/TLR4-induced corneal inflammation. Corneas of MaFIA mice were stimulated with LPS and treated ± AP20187 to understand the role of macrophages and dendritic cells in development of corneal inflammation.


Ezratty, E. J. et al. (2009) J. Cell Biol. 187(5):733–747. Clathrin mediates integrin endocytosis for focal adhesion disassembly in migrating cells. AP20187 was used to crosslink and thereby disrupt clathrin function, inhibit focal adhesion disassembly, and decrease the rate of cell migration.


Markey, K. A. et al. (2009) Blood 113(22):5644–5649. Conventional dendritic cells are the critical donor APC presenting alloantigen after experimental bone marrow transplantation. Conditional deletion of conventional dendritic cells (cDCs), plasmacytoid DC (pDCs), macrophages, or B cells was used to demonstrate that donor cDCs are the critical population presenting alloantigen after bone marrow transplantation.


Roostaei, A., Côté, S., and Roucou X. (2009) J. Biol. Chem. 284(45):30907–30916. Aggregation and amyloid fibril formation induced by chemical dimerization of recombinant prion protein in physiological-like conditions. The authors treated a chimeric cellular protein (PrP(C)) with AP20187 to cause a rapid conformational change and simultaneous aggregation of the protein, suggesting that dimerization of PrP(C) may initiate the pathogenesis of prion diseases.


2008 Citations


Oyadomari, S. et al. (2008) Cell Metab. 7(6):520–532. Dephosphorylation of translation initiation factor 2a enhances glucose tolerance and attenuates hepatosteatosis in mice. Transgenic mice expressing the cytosolic PERK kinase domain fused to an artificial dimerization domain were treated with AP20187 to activate the integrated stress response in the liver.


Steel, C. D. et al. (2008) Lab Anim. (NY) 37(1):26–32. Comparison of the lateral tail vein and the retro-orbital venous sinus as routes of intravenous drug delivery in a transgenic mouse model. To compare lateral tail vein and retro-orbital venous sinus injections, MaFIA mice were injected with AP20187, and macrophage depletion was compared for the lung, spleen, bone marrow, and peritoneal exudate cells. Both injection routes were similarly effective.


2007 Citations

Acevedo, V. D. et al. (2007) Cancer Cell 12(6):559–571. Inducible FGFR-1 activation leads to irreversible prostate adenocarcinoma and an epithelial-to-mesenchymal transition. Activation of FGFR1 with chemical inducers of dimerization (CID) led to highly synchronous, step-wise progression to adenocarcinoma that is linked to an epithelial-to-mesenchymal transition (EMT) and implicated FGFR1 in prostate cancer progression.


Deng, Y. et al. (2007) Am. J. Physiol. Cell Physiol. 293(4):C1404–C1411. MEKK3 is required for endothelium function but is not essential for tumor growth and angiogenesis. AP20187 was used to artificially activate Tie2 in either wild-type or MEKK3-deficient cells and determine that MEKK3 is critical for Ang1/Tie2 signaling to the p38 MAPK pathway.

Dong, Z. et al. (2007) Exp. Cell Res. 313(16):3645–3657. Level of endothelial cell apoptosis required for a significant decrease in microvessel density. Inducible caspase-9 was used to understand the effects of endothelial cell apoptosis on blood vessel generation.

Gazdoiu, S. et al. (2007) Mol. Cell Biol. 27(20):7041–7052. Human Cdc34 employs distinct sites to coordinate attachment of ubiquitin to a substrate and assembly of polyubiquitin chains. The chemical dimerizer AP20187 was used activate Cdc34 and study its role in polyubiquitination.

Goggin, K. et al. (2007) J. Neurochem. 102(4):1195–1205. Aggregation of cellular prion protein is initiated by proximity-induced dimerization. Inducible oligomerization was used to test if, in the absence of any infectious prion particles, the encounter between PrP(C) molecules may trigger its aggregation in neuronal cells.

Isaacs, H. V. et al. (2007) Biol. Cell 99(3):165–173. FGF4 regulates blood and muscle specification in Xenopus laevis. The authors used a drug inhibitor of FGF signalling and an inducible form of FGF receptor 1 to identify a period of competence during late blastula and gastrula stages when FGF signalling acts to regulate blood versus muscle specification.


Miyake, Z. et al. (2007) Mol. Cell Biol. 27(7):2765–2776. Activation of MTK1/MEKK4 by GADD45 through induced N-C dissociation and dimerization-mediated trans autophosphorylation of the MTK1 kinase domain. An inducible version of MTK1 was used to determine that GADD45 binding leads to the activation of the kinase catalytic domain of MTK1.

Niu, H. et al. (2007) Mol. Cell Biol. 27(15):5456–5467. Mek1 kinase is regulated to suppress double-strand break repair between sister chromatids during budding yeast meiosis. Using a version of Mek1 that can be conditionally dimerized during meiosis, Mek1 function was shown to be promoted by dimerization, but DSBs and Mek1 recruitment to the meiosis-specific chromosomal core protein Red1 were also required for Mek1 activation.

Nourse, M. B. et al. (2007) Lab. Invest. 87(8):828–835. Selective control of endothelial cell proliferation with a synthetic dimerizer of FGF receptor-1. Human umbilical vein endothelial cells and human microvascular endothelial cells expressing an inducible FGF receptor were used to study the effects of synthetic receptor-dimerizing ligands.


2007 Citations...continued

Sequeira, S. J. et al. (2007) PLoS ONE 2(7):e615. Inhibition of proliferation by PERK regulates mammary acinar morphogenesis and tumor formation. An inducible version of the ER kinase PERK was used to study PERK’s role in limiting MCF10A mammary epithelial cell proliferation during acinar morphogenesis, as well as in preventing mammary tumor formation in vivo.

Shah, V. R. et al. (2007) Genesis 45(4):194–199. Double-inducible gene activation system for caspase 3 and 9 in epidermis. The authors developed a double inducible model containing both RU486 and AP20187, which in addition to inducing caspase activation, has potential applicability to other genes encoding proteins that require a dimerization event for activation.


Tokuo, H., Mabuchi, K., and Ikebe, M. (2007) J. Cell Biol. 179(2):229–238. The motor activity of myosin-X promotes actin fiber convergence at the cell periphery to initiate filopodia formation. Using a dimer-inducing technique, the authors show that the motor function of myoX, and not the cargo function, is critical for initiating filopodia formation.


Xian, W., Schwertfeger, K. L., and Rosen, J. M. (2007) Mol. Endocrinol. 21(4):987–1000. Distinct roles of fibroblast growth factor receptor 1 and 2 in regulating cell survival and epithelial-mesenchymal transition. A chemically inducible FGFR (iFGFR) dimerization system was combined with an in vitro three-dimensional HC11 mouse mammary epithelial cell culture model in order to examine the separate roles of FGFR1 and FGFR2 signaling in polarized epithelia.

2006 Citations


Burnett, S. H. et al. (2006) J. Surg. Res. 131(2):296–301. Development of peritoneal adhesions in macrophage depleted mice. A mouse model was developed to study the induction and repair of peritoneal adhesions, based on the finding that such adhesions develop upon AP20187-mediated depletion of macrophages in MaFIA mice.


2006 Citations…continued

Goffin, L. et al. (2006) Mol. Biol. Cell 17(12):5309–5323. The unfolded protein response transducer Ire1p contains a nuclear localization sequence recognized by multiple β importins. AP20187 was used to dimerize the Ire1p transmembrane receptor kinase/endonuclease, which transduces the unfolded protein response (UPR) from the endoplasmic reticulum (ER) to the nucleus in Saccharomyces cerevisiae.

Hirate, Y. and Okamoto, H. (2006) Curr. Biol. 16(4):421–427. Canopy1, a novel regulator of FGF signaling around the midbrain-hindbrain boundary in zebrafish. AP20187-induced dimerization of FGFR1 was used to demonstrate that expression of Canopy1 is essential for normal FGF signaling in zebrafish embryos. The inducible FGFR1 gene was injected as mRNA into a specific area of the brain and AP20187 was added directly to the embryos.


Schwertfeger, K. L. et al. (2006) Cancer Res. 66(11):5676–5685. A critical role for the inflammatory response in a mouse model of preneoplastic progression. Transgenic mice expressing an AP20187-inducible fibroblast growth factor receptor-1 (iFGFR1) were used to examine the role of the microenvironment in early stages of tumorigenesis. These mice were also crossed with MaFIA mice to study the effects of macrophage depletion on iFGFR1-mediated phenotypes.


Umeda, K. et al. (2006) Cell 126(4):741–754. ZO-1 and ZO-2 independently determine where claudins are polymerized in tight-junction strand formation. When a truncated version of the tight junction protein ZO-1 was forcibly recruited to lateral membranes and dimerized, claudins were dramatically polymerized.


Witt, A. E. et al. (2006) J. Proteome Res. 5(3):599–610. Functional proteomics approach to investigate the biological activities of cDNAs implicated in breast cancer. The functional activity of a subset of the Breast Cancer 1000 collection was evaluated in cell-based assays that monitor changes in cell proliferation, migration, and morphogenesis in MCF-10A mammary epithelial cells expressing a variant of ErbB2 that can be inducibly activated through dimerization.

Xiao, H. et al. (2006) J. Biomol. Screen. 11(3):225–235. Establishment of a cell model based on FKBP12 dimerization for screening of FK506-like neurotrophic small molecular compounds. The AP20187-mediated homodimerization system was used to screen for novel FK506-like small molecules. Compounds were screened for the ability to block apoptosis caused by forced dimerization of mBax.

2005 Citations

Abell, A. N. and Johnson, G. L. (2005) J. Biol. Chem. 280(43):35793–35796. **MEKK4 is an effector of the embryonic TRAF4 for JNK activation.** Uses AP20187 to show that oligomerization of MEKK4 is sufficient to activate JNK.

Blau, C. A. et al. (2005) J. Biol. Chem. 280(44):36642–36647. **γ-Globin gene expression in chemical inducer of dimerization (CID)-dependent multipotential cells established from human β-globin locus yeast artificial chromosome (β-YAC) transgenic mice.** Developed cells that can be used to screen for inducers of gamma-globulin expression by using an AP20187-inducible mpl construct to drive proliferation of bone marrow cells derived from beta-YAC transgenic mice.


Cheng, J. et al. (2005) J. Biol. Chem. 280(14):13477–13482. **Dimerization through the catalytic domain is essential for MEKK2 activation.** Uses AP20187 to demonstrate that oligomerization of MEKK2 leads to its activation.


Frêche, B. et al. (2005) J. Biol. Chem. 280(44):36584–36591. **Inducible dimerization of RET reveals a specific AKT deregulation in oncogenic signaling.** Uses AP20187-mediated dimerization to study downstream effects of activating the receptor tyrosine kinase RET.


Gouzi, J. Y. et al. (2005) J. Cell Sci. 118(Pt 24):5811–5823. **Role of the subcellular localization of ALK tyrosine kinase domain in neuronal differentiation of PC12 cells.** Uses AP20187 to control the dimerization and activation of the membrane tyrosine kinase ALK.

Hanks, B. A. et al. (2005) Nat. Med. 11(2):130–137. **Re-engineered CD40 receptor enables potent pharmacological activation of dendritic-cell cancer vaccines in vivo.** Dendritic cell activation mediated by an AP20187-inducible CD40 receptor results in more potent T-cell effector responses in mice and may lead to more potent human cancer vaccines.


Larrivée, B. et al. (2005) J. Immunol. 175(5):2890–2899. **Minimal contribution of marrow-derived endothelial precursors to tumor vasculature.** Uses an AP20187-inducible VEGF receptor 2 to demonstrate that the VEGFR-2 pathway is not sufficient for the recruitment and/or expansion of endothelial progenitor cells in mice.


Lupo, G. et al. (2005) Development 132(7):1737–1748. **Dorsoventral patterning of the Xenopus eye: a collaboration of retinoid, hedgehog and FGF receptor signaling.** Uses an AP20187-inducible FGF receptor 1 to explore the role of the FGFR1 signaling pathway in dorsoventral patterning of the Xenopus eye.


2005 Citations…continued


2004 Citations


2004 Citations…continued


Richard, R. E. et al. (2004) Mol. Ther. 10(4):730–740. Differences in F36VMpl-based in vivo selection among large animal models. AP20187-mediated oligomerization of mpl leads to only a modest expansion of hematopoietic cells in baboons, in contrast to what was seen previously in mice.


2003 Citations


2003 Citations...continued


Freeman, K. W. et al. (2003) Cancer Res. 63(19):6237–6243. Conditional activation of fibroblast growth factor receptor (FGFR) 1, but not FGFR2, in prostate cancer cells leads to increased osteopontin induction, extracellular signal-regulated kinase activation, and in vivo proliferation. Uses an AP20187-inducible FGFR1 to demonstrate its role in signaling and its ability to promote growth of prostate tumor cells in vivo.

Freeman, K. W. et al. (2003) Cancer Res. 63(23):8256–8263. Inducible prostate intraepithelial neoplasia with reversible hyperplasia in conditional FGFR1-expressing mice. Uses transgenic mice containing an AP20187-inducible FGFR1 to show that the development and progression of key pathologic changes seen in early-stage prostate cancer are directly dependent on FGFR1 activation.

Godbey, W. T. and Atala, A. (2003) Gene Ther. 10(17):1519–1527. Directed apoptosis in Cox-2-overexpressing cancer cells through expression-targeted gene delivery. AP20187-inducible caspase-3 (or -9) was used to selectively induce apoptosis in tumor cells that overexpress Cox-2, including cells that are typically resistant to apoptosis.


2003 Citations…continued


2002 Citations


Chang, D. W. et al. (2002) EMBO J. 21(14):3704–3714. c-FLIP(L) is a dual function regulator for caspase-8 activation and CD95-mediated apoptosis. Rapamycin-mediated heterodimerization and AP20187-mediated homodimerization were used to explore the role of c-FLIP-L in the CD95-mediated apoptotic signaling pathway.


Feng, H. et al. (2002) Blood 100(12):4108–4115. Stressed apoptotic tumor cells stimulate dendritic cells and induce specific cytotoxic T cells. Uses AP20187-mediated oligomerization of Fas to induce apoptosis to explore how the immune system distinguishes stressed from non-stressed apoptotic tumor cells.


2002 Citations…continued


Zhao, S. et al. (2002) EMBO J. 21(9):2159–2167. JAK2, complemented by a second signal from c-kit or flt-3, triggers extensive self-renewal of primary multipotential hematopoietic cells. AP20187-induced homodimerization and activation of a cytoplasmic JAK2 signaling domain, together with addition of either c-kit or flt-3 ligands, can trigger self-renewal of primary multipotential hematopoietic progenitor cells.

2001 Citations
Feng, H. et al. (2001) Blood 97(11):3505–3512. Stressed apoptotic tumor cells express heat shock proteins and elicit tumor-specific immunity. Uses AP20187-mediated dimerization of Fas to show that apoptotic tumor cells can be made immunogenic if they are heat-stressed prior to apoptotic induction.


Moulder, S. L. et al. (2001) Cancer Res. 61(24):8887–8895. Epidermal growth factor receptor (HER1) tyrosine kinase inhibitor ZD1839 (Iressa) inhibits HER2/neu (erbB2)-overexpressing breast cancer cells in vitro and in vivo. Uses AP1510-mediated activation of EGFR or HER2 receptor tyrosine kinases to demonstrate the relative specificity of the tyrosine kinase inhibitor Iressa for EGFR.


2001 Citations...continued


Zeng, H. et al. (2001) *Blood* 98(2):328–334. Receptor specificity in the self-renewal and differentiation of primary multipotent hemopoietic cells. AP20187-mediated oligomerization of Mpl, the G-CSF receptor, or Flt-3 is sufficient to induce growth of BaF3 cells, but only dimerization of Mpl induces mouse hematopoietic cell self renewal.

2000 Citations


Inohara, N. et al. (2000) J. Biol. Chem. 275(36):27823–27831. An induced proximity model for NF-kappaB activation in the Nod1/RICK and RIP signaling pathways. AP1510-mediated oligomerization of Nod1, RICK, RIP and IKK-alpha, -beta, or gamma is sufficient to activate NF-kappaB.


1999 Citations


Baud, V. *et al.* (1999) *Genes Dev.* 13(10):1297–1308. **Signaling by proinflammatory cytokines: oligomerization of TRAF2 and TRAF6 is sufficient for JNK and IKK activation and target gene induction via an amino-terminal effector domain.** FK1012-mediated oligomerization of TRAF2 or TRAF6 activates multiple downstream targets, including JNK and IKK.


1998 Citations


1998 Citations…continued


1997 Citations


Blau, C. A. et al. (1997) Proc. Natl. Acad. Sci. USA 94(7):3076–3081. A proliferation switch for genetically modified cells. The first demonstration of dimerizers to specifically and reversibly stimulate the proliferation of a population of engineered cells. FK1012-mediated dimerization of the signaling domain of the erythropoietin receptor is shown to stimulate the proliferation of cells normally dependent on IL-3 for growth.


1996 Citations


1995 Citations


1994 Citations


1993 Citations