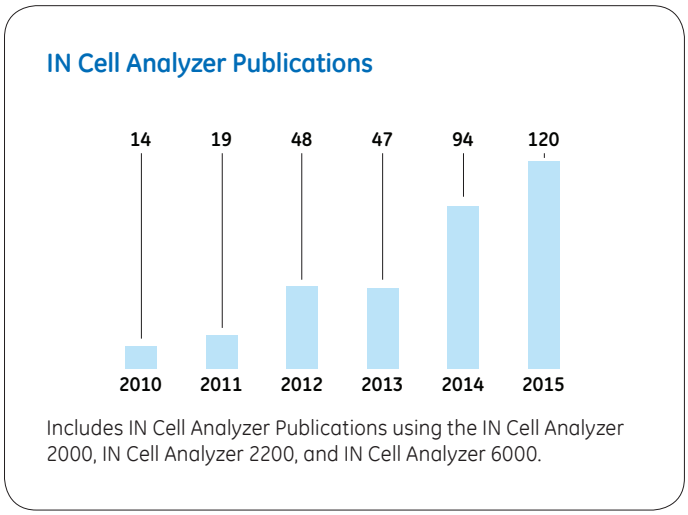
Selected IN Cell Analyzer publications

Publications utilizing the IN Cell Analyzer 2000, IN Cell Analyzer 2200, and IN Cell Analyzer 6000 have increased eight fold in the past five years. Here, a selection of 79 papers from the last two years is featured and categorized according to application. Trending applications include: 3-D biology, regenerative medicine, neurobiology, drug discovery, and nanotechnology.*



Includes IN Cell Analyzer Publications using the IN Cell Analyzer 2000, IN Cell Analyzer 2200, and IN Cell Analyzer 6000.

Alzheimer's disease

1. Fu, A. *et al.* IL-33 ameliorates Alzheimer's disease-like pathology and cognitive decline. *Proc Natl Acad Sci USA* **113(9)**, E2705-E2713 (2016), doi:10.1073/pnas.1604032113.
2. Imaizumi, K. *et al.* Controlling the regional identity of hPSC-derived neurons to uncover neuronal subtype specificity of neurological disease phenotypes. *Stem Cell Reports* **5(6)**, 1010-1022 (2015), doi: 10.1016/j.stemcr.2015.10.005.
3. Nagashima, T. *et al.* Feedforward regulation of mRNA stability by prolonged extracellular signal-regulated kinase activity. *FEBS J* **282**, 613-629 (2015), doi: 10.1111/febs.13172.

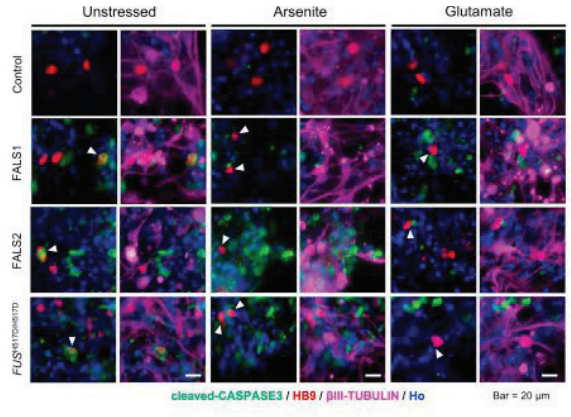
Apoptosis

1. Lewinska, A. *et al.* Capsaicin-induced genotoxic stress does not promote apoptosis in A549 human lung and DU145 prostate cancer cells. *Mutat Res* **779,** 23-34 (2015), doi:10.1016/j.mrgentox.2015.02.003.
2. Lewinska, A. *et al.* Diosmin induces genotoxicity and apoptosis in DU145 prostate cancer cell line. *Toxicol In Vitro* **29**, 417-425 (2015), doi: 10.1016/j.tiv.2014.12.005.

*Many publications could have been placed into several categories, but are only listed once. Please look through related categories for completeness.

Amyotrophic lateral sclerosis

1. Frakes, A. *et al.* Microglia induce motor neuron death via the classical NFκB pathway in Amyotrophic Lateral Sclerosis. *Neuron* **81(5)**, 1009-1023 (2014), doi: 10.1016/j.neuron.2014.01.013.
2. Ichiyangi, N. *et al.* Establishment of in vitro FUS-associated familial amyotrophic lateral sclerosis model using human induced pluripotent stem cells. *Stem Cell Reports* **6(4)**, 496-510 (2016), doi: 10.1016/j.stemcr.2016.02.011.



Science: Amyotrophic lateral sclerosis (ALS) is a debilitating disease of the body's motor neurons, yet we lack understanding of the cellular and molecular mechanisms that trigger its onset. To study an ALS model, an apoptosis assay in induced pluripotent stem cell (iPSC) derived motor neurons is shown. HP9-positive motor neurons are shown in red, cleaved-CASPASE3 is shown in green to assay apoptosis, βII-TUBULIN marks immature neurons in pink, and nuclei were stained with Hoechst in blue. This paper advances tools for studying ALS by developing an assay to derive motor neurons from patients.

Technology: Over 10,000 cells per well were imaged on an IN Cell Analyzer 6000 by acquiring 25 fields of view per well with a 20x objective. IN Cell Developer segmented nuclei and neurons were identified by positive HP9 staining. Then, the cell ratio of cleaved-CASPASE3-positive cells to βII-positive neurons or HB9-positive motor neurons was determined.

Title: Establishment of in vitro FUS-associated familial amyotrophic lateral sclerosis model using human induced pluripotent stem cells

Authors: N. Ichiyangi, K. Fujimori, M. Yano, C Ishihara-Fujisaki, T Sone, T Akigama, Y Okada, W Akamatsu, T Matsumoto, M Ishikawa, Y Nishimoto, Y Ishihara, T Sakamura, T. Yamamoto, H Tsuji, N Suzuki, H Warita, M Aoki, H. Okano

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3. Li, Q, *et al.* The cleavage pattern of TDP-43 determines its rate of clearance and cytotoxicity. *Nat Commun* **6(6183)**, 1-12 (2015), doi:10.1038/ncomms7183.

Autophagy

1. Cai, Y. *et al.* Loss of chromosome 8p governs tumor progression and drug response by altering lipid metabolism. *Cancer Cell* **29,** 751-766 (2016), doi: 10.1016/j.ccell.2016.04.003.
2. Ejlerskov, P. *et al.* Lack of neuronal IFN-β-IFNAR causes Lewy Body and Parkinson's disease-like Dementia. *Cell* **163(2)**, 324-339 (2015), doi:10.1016/j.cell.2015.08.069.

Cancer

1. Baietti, M. *et al.* OTUB1 triggers lung cell development by inhibiting RAS monoubiquitination. *EMBO Mol Med* **8**, 288-303 (2016), doi:10.15252/emmm.201505972.
2. Bao, X. *et al.* Small molecule schweinfurthins selectively inhibit cancer cell proliferation and mTOR/AKT signaling by interfering with trans-Golgi-network trafficking. *Cancer Biol Ther* **16(4)**, 589-601 (2015), doi: 10.1080/15384047.2015.1019184.
3. Chun, S. *et al.* Targeted inhibition of histone deacetylases and hedgehog signaling suppress tumor growth and homologous recombination in aerodigestive cancers. *Am J Cancer Res* **5(4)**, 1337-1352 (2015).
4. Daemen, A. *et al.* Metabolite profiling stratifies pancreatic ductal adenocarcinomas into subtypes with distinct sensitivities to metabolic inhibitors. *Proc Natl Acad Sci USA* E4410-E4417 (2015), doi:10.1073/pnas.1501605112.
5. Duong, D. *et al.* Pronounced peptide selectivity for melanoma through tryptophan end-tagging. *Sci Rep* **6(24952)**, 1-17 (2016), doi: 10.1038/srep24952.
6. Gonçalves, I. *et al.* Bacteria-targeted biomaterials: Glycan-coated microspheres to bind *Helicobacter pylori*. *Acta Biomater* **33**, 40-50 (2016), doi: 10.1016/j.actbio.2016.01.029.
7. Kasai, N, *et al.* Effect of antigen-dependent clearance on pharmacokinetics of anti-heparin-binding EGF-like growth factor (HB-EGF) monoclonal antibody. *mAbs* **6(5)**, 1220-1228 (2014), doi: 10.4161/mabs.29792.
8. Kume, K. *et al.* α-Amanitin restrains cancer relapse from drug-tolerant cell subpopulations via TAF15. *Sci Rep* **6(25895)**, 1-15 (2016), doi: 10.1038/srep25895.
9. Li, S. *et al.* Formononetin promotes angiogenesis through the estrogen receptor alpha-enhanced ROCK pathway. *Sci Rep* **5(16815)**, 1-17 (2015), doi: 10.1038/srep16815.
10. Liu, L. *et al.* Inhibition of the p53/hDM2 protein-protein interaction by cyclometallated iridium (III) compounds. *Oncotarget* **7(12)**, 13965-13975 (2016), doi: 10.18632/oncotarget.7369.
11. Misumi, K. *et al.* Enhanced gefitinib-induced repression of the epidermal growth factor receptor pathway by ataxia telangiectasia-mutated kinase inhibition in non-small-cell lung cancer cells. *Cancer Sci* **107(4)**, 444-451 (2016), doi:10.1111.cas.12899.
12. Nakamura, K. *et al.* DNA methyltransferase inhibitor Zebularine induces human cholangiocarcinoma cell death through alteration of DNA methylation status. *PLOS One* **10(3)**, e0120545, 1-21 (2015), doi: 10.1371/journal.pone.0120545.
13. Oku, Y. *et al.* Small molecules inhibiting the nuclear localization of YAP/TAZ for chemotherapeutics and chemosensitizers against breast cancers. *FEBS Open Bio* **5**, 542-549 (2015), doi: 10.1016.j.fob.2015.06.007.
14. Pinto, A. *et al.* Ionizing radiation modulates human macrophages towards a pro-inflammatory phenotype preserving their pro-invasive and pro-angiogenic capacities. *Sci Rep* **6(18765)**, 1-15 (2016), doi: 10.1038/srep18765.
15. Sugimoto, K. *et al.* Discovery of a drug targeting microenvironmental support for lymphoma cells by screening using patient-derived xenograft cells. *Sci Rep* **5(13054)**, 1-12 (2015), doi: 10.1038/srep13054.
16. Wang, L. *et al.* A novel Danshensu derivative prevents cardiac dysfunction and improves the chemotherapeutic efficacy of doxorubicinin breast cancer cells. *J Cell Biochem* **117**, 94-105 (2016), doi:10.1002/jcb.25253.
17. Wang, Y. *et al.* Particle size tailoring of ursolic acid nanosuspensions for improved anticancer activity by controlled antisolvent precipitation. *Int J Pharm* **494**, 479-489 (2015), doi: 10.1016/j.ijpharm.2015.08.052.
18. Wehbe, M. *et al.* Nanoscale reaction vessels designed for synthesis of copper-drug complexes suitable for preclinical development. *PLOS One* **11(4)**, e0153416, 1-16 (2015), doi: 10.1371/journal.pone.0153416.

Cardiomyocytes

1. Clements, M. *et al.* High-throughput multi-parameter profiling of electrophysiological drug effects in human embryonic stem cell derived cardiomyocytes using multi-electrode arrays. *Toxicol Sci* **140(2)**, 445-461 (2014), doi: 10.1093/toxsci/kfu084.
2. Li, J. *et al.* Profiling of nutrient transporter expression in human stem cell-derived cardiomyocytes exposed to tyrosine kinase inhibitor anticancer drugs using RBD ligands. *J Biomol Screen* **19(8)**, 1185-1192 (2014), doi: 10.1177/1087057114533724.

Cell therapy

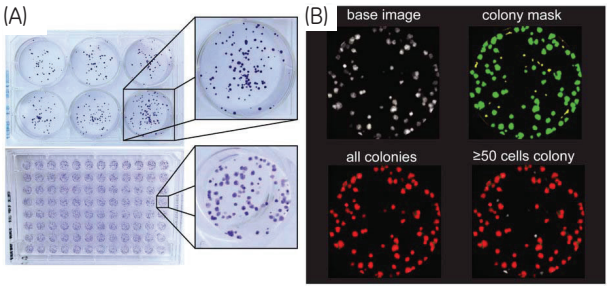
1. Kusakawa, S. *et al.* Ultra-sensitive detection of tumorigenic cellular impurities in human cell-processed therapeutic products by digital analysis of soft agar colony formation. *Sci Rep* **5(17892)**, 1-11 (2015), doi:10.1038/srep17892.

DNA damage

1. Kubota, Y. *et al.* SNF2H interacts with XRCC1 and is involved in repair of H_2O_2-induced DNA damage. *DNA Repair* **43**, 69-77 (2016), doi: 10.1016/j.dnarep.2016.03.010.
2. Leung, A, *et al.* 3' Phosphoadenosine 5'phosphosulfate synthase 1 (PAPSS1) knockdown sensitizes non-small cell lung cancer cells to DNA damaging agents. *Oncotarget* **6(19)**, 17161-17177 (2015).
3. Sasatini, M. *et al.* RAD18 activates the G2/M checkpoint through DNA damage signaling to maintain genome integrity after ionizing radiation exposure. *PLOS One* **10(2)**, e0117845 (2015), doi: 10.1371/journal.pone.0117845.

Drug discovery

1. Bondar, O. *et al.* Intracellular delivery of VEGF165 encoding gene therapeutic using trifunctional copolymers of ethylene oxide and propylene oxide. *Eur Polym J* **68**, 680-686 (2015), doi:10.1016/j.eurpolymj.2015.03.042.



Science: To examine efficacy of proton beam therapy as an alternative to traditional X-ray based radiation treatment, high-throughput clonogenic survival assays were performed. Specifically, high-throughput clonogenic assays on the IN Cell Analyzer 6000 were used to compare to the more traditional manual analysis. Panel B shows data from the IN Cell Analyzer with and without image processing masks. This paper advances cancer treatment by directly comparing a new therapy to traditional X-ray treatment.

Technology: After colony formation, cells were fixed, stained and imaged on the IN Cell Analyzer 6000 to identify colonies containing ≥ 50 cells. Four overlapping fields of view were acquired with a 4 x 0.20 NA objective, and IN Cell Developer Toolbox software was used to stitch the images together. Masks were generated as shown above.

Title: Spatial mapping of the biologic effectiveness of scanned particle beams: towards biologically optimized particle therapy

Authors: F. Guan, L. Bronk, U. Tilt, S. Lin, D. Mirkovic, M Kerr, X. Zhu, J. Dinh, M. Sobieski, C. Stephan, C. Peeler, R. Taleei, R. Mohan, D. Grosshans

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2. Bradley, M. *et al.* Potent and efficacious inhibition of CXCR2 signaling by biparatopic nanobodies combining two distinct modes of action. *Mol Pharmacol* **87**, 251-262 (2015), doi: 10.1124/mol.114.094821.
3. Endo, K. *et al.* High-resolution identification and separation of living cell types by multiple microRNA-responsive synthetic mRNAs. *Sci Rep* **6(21991)**, 1-8 (2016), doi: 10.1038/srep21991.
4 Guan, F. *et al.* Spatial mapping of the biologic effectiveness of scanned particle beams: towards biologically optimized particle therapy. *Sci Rep* **5(9850)**, 1-10 (2015), doi: 10.1038/srep09850.
5. Guo. L. *et al.* Human $CD34^+$ progenitor hematopoiesis in liquid culture for in vitro assessment of drug-induced myelotoxicity. *Toxicol In Vitro* **31**, 103-113 (2016), doi: 10.1016/j.tiv.2015.11.017.
6. Lin, S. *et al.* A high content clonogenic survival drug screen identifies MEK inhibitors as potent radiation sensitizers for KRAS mutant non-small-cell lung cancer. *J Thorac Oncol* **9(7)**, 965-973 (2014), doi: 10.1097/JTO.0000000000000199.
7. Summers, H. *et al.* Multiscale benchmarking of drug delivery vectors. *Nanomedicine* **12(7)**, 1843-1851 (2016), doi:10.1016/j.nano.2016.03.006.
8. Trefely, S. *et al.* Kinome screen identifies PFKFB3 and glucose metabolism as important regulators of the Insulin/Insulin-like Growth Factor (IGF)-1 signaling pathway. *J Biol Chem* **290(43)**, 25834-25846 (2015), doi: 10.1074/jbc.M115.658815.
9. Xiao, H. and Wang L. Effects of X-shaped reduction-sensitive amphiphilic block copolymer on drug delivery. *Int J Nanomedicine* **10**, 5309-5325 (2015), doi: 10.2147/IJN.S85230.

Heart disease

1. Lewinska, A. *et al.* Curcumin induces oxidation-dependent cell cycle arrest mediated by SIRT7 inhibition of rDNA transcription in human aortic smooth muscle cells. *Toxicol Lett* **233**,227-238 (2015), doi: 10.1016/j.toxlet.2015.01.019.

3-D biology

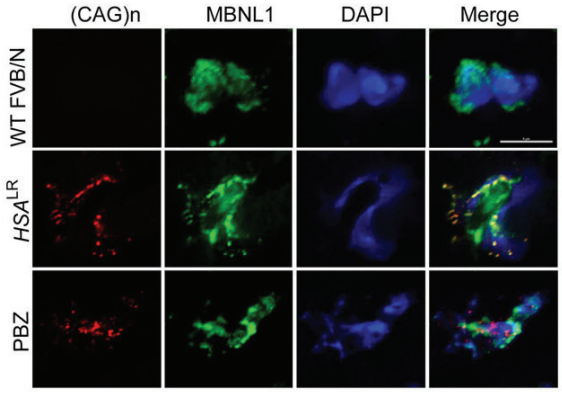
1. Danahay, H. *et al.* Notch2 is required for inflammatory cytokine-driven goblet cell metaplasia in the lung. *Cell Rep* **10**, 239-252 (2015), doi:10.1016/j.celrep.2014.12.017.
2. Li, L. *et al.* High-throughput imaging: Focusing in on drug discovery in 3D. *Methods* **96**, 97-102 (2016), doi: 10.1016/j.ymeth.2015.11.013.
3. Tenga, A. *et al.* Regulation of nuclear receptor Nur77 by miR-124. *PLOS One* **11(2),** e0148433, 1-22 (2016), doi: 10.1371/journal.pone.0148433.

Kidney disease

1. Shimomura, A, *et al.* Dietary L-lysine prevents arterial calcification in adenine-induced uremic rats. *J Am Soc Nephrol* **25(9)**, 1954-65 (2014), doi: 10.1681/ASN.2013090967.

Myotonic dystrophy

1. Chen, G. *et al.* Phenylbutazone induces expression of MBNL1 and suppresses formation of MBNL1-CUG RNA foci in a mouse model of myotonic dystrophy. *Sci Rep* **6(25317)**, 1-11 (2016), doi: 10.1038/srep25317.



Science: RNA FISH/IF experiment on mouse quadriceps muscle sections showing the effect of phenylbutazone on the association of MBNL1, a splicing regulator, with nuclear foci. CAG repeats are shown in red, MBNL1 is shown in green, and the nuclei are stained blue with DAPI. This study advances our understanding of a mouse model of myotonic dystrophy and shows the promise of phenylbutazone as a therapeutic agent.

Technology: The IN Cell Analyzer 6000 was used to image 6µm sections of the quadriceps muscle from six mice. Multiple randomly selected fields of view were collected to quantify the association of MBNL1 with nuclear foci.

Title: Phenylbutazone induces expression of MBNL1 and suppresses formation of MBNL1-CUG RNA foci in a mouse model of myotonic dystrophy

Authors: G. Chen, A. Masuda, H Konishi, B. Ohkawara, M. Ito, M. Kinoshita, H. Kiyama, T. Matsuda, K. Ohno

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Nanotechnology

1. Mytych, J. *et al.* Nanoparticle-mediated decrease of lamin B1 pools promotes a TRF protein-based adaptive response in cultured cells. *Biomaterials* **53**, 107-116 (2015), doi: 10.1016/j.biomaterials.2015.02.072.
2. Mytych, J. *et al.* Prolonged effects of silver nanoparticles on p53/p21 pathway-mediated proliferation, DNA damage response, and methylation parameters in HT22 hippocampal neuronal cells. *Mol Neurobiol* (2016), doi: 10.1007/s12035-016-9688-6.
3. Ribeiro, A. *et al.* Trojan-like internalization of anatase titanium dioxide nanoparticles by human osteoblast cells. *Sci Rep* **6(23615)**, 1-11 (2016), doi: 10.1038/srep23615.
4. Tzur-Balter, A. *et al.* Mechanism of erosion of nanostructured porous silicon drug carriers in neoplastic tissues. *Nat Commun* **6(6208)**, 1-8 (2015), doi: 10.1038/ncomms7208.
5. Zielinski, J. *et al.* Evaluation of endocytosis of silica particles used in biodegradable implants in the brain. *Nanomedicine* **12**, 1603-1613 (2016), doi: 10.1016/j.nano.2016.02.009.

Neurobiology

1. Gorska, M. *et al.* DNA strand break induced by nuclear hijacking of neuronal NOS as an anti-cancer effect of 2-methoxyestradiol. *Oncotarget* **6(17)**, 15449-15463 (2015).
2. Miller, K. *et al.* Automated measurement of fast mitochondrial transport in neurons. *Front Cell Neurosci* **9(435)**, 1-17 (2015), doi: 10.3389/fncel.2015.00435.
3. Srikanth, P. *et al.* Genomic DISC1 disruption in hiPSCs alters Wnt signaling and neural cell fate. *Cell Rep* **12**, 1414-1429 (2015), doi: 10.1016/j.celrep.2015.07.061.
4. Tan, Y. *et al.* Endogenous docosahexaenoic acid (DHA) prevents Aβ1-42 oligomer-induced neuronal injury. *Mol Neurobiol* (2015), doi: 10.007/s12035-015-9224-0.
5. Thorne, N. *et al.* High-throughput phenotypic screening of human astrocytes to identify compounds that protect against oxidative stress. *Stem Cells Transl Med* **5**, 613-627 (2016), doi: 10.5966/sctm.2015-0170.
6. Yoshida, M. *et al.* Modeling the early phenotype at the neuromuscular junction of spinal muscular atrophy using patient-derived iPSCs. *Stem Cell Reports* **4**, 561-568 (2015), doi: 10.1016/j.stemcr.2015.02.010.

Parkinson's disease

1. Prusiner, S. *et al.* Evidence for β-synuclein prions causing multiple system atrophy in humans with Parkinsonism. *Proc Natl Acad Sci USA* **112(38)**, E5308-E5317 (2015), doi: 10.1073/pnas.1514475112.

Prions

1. Couceiro, J. *et al.* Sequence-dependent internalization of aggregating peptides. *J Biol Chem* **290(1)**, 242-258 (2015), doi: 10.1074/jbc.M114.586636.

Regenerative medicine

1. Czysz, K. *et al.* Pluripotency genes in human embryonic stem cells during definitive endoderm derivation and increases the proficiency of hepatic differentiation. *PLOS One* **10(2)**, e0117689 (2015), doi: 10.1371/journal.pone.0117689.
2. Dumevska, B. *et al.* Derivation of human embryonic stem cell line Genea019. *Stem Cell Res* **16(2)**, 397-400 (2016), doi:10.1016/j.scr.2016.02.008.
3. Garcia, T. *et al.* RBPJ in mouse Sertoli cells is required for the proper regulation of the testis stem cell niche. *Development* **141(23)**, 4468-4478 (2014), doi: 10.1242/dev.113969.

4. Goldshmid, R. *et al.* Steric interference of adhesion supports *in vitro* chrondrogenesis of mesenchymal stem cells on hydrogels for cartilage repair. *Sci Rep* **5(12607)**, 1-13 (2015), doi: 10.1038/srep12607.
5. Ozeki, N. *et al.* Wnt16 signaling is required for IL-1β-induced matrix metalloproteinase-13 regulated proliferation of human stem cell derived osteoblastic cells. *Int J Mol Sci* **17**, (221) 1-14 (2016), doi:10.3390/ijms17020221.

Toxicology

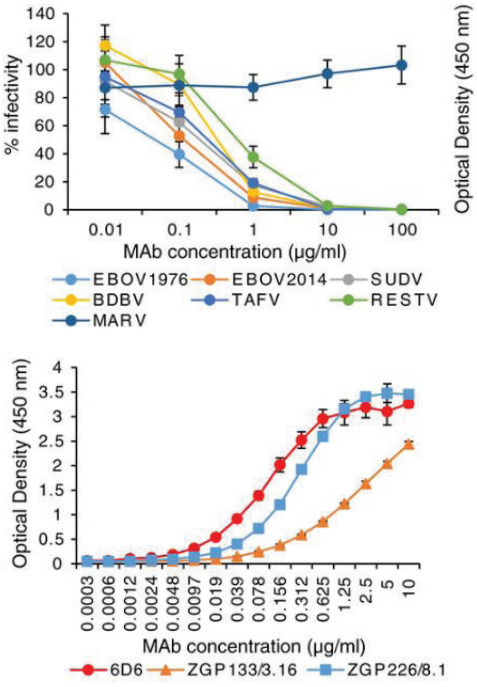
1. Farcal, L. *et al.* Comprehensive *in vitro* toxicity testing of a panel of representative oxide nanomaterials: First steps towards an intelligent testing strategy. *PLOS One* **10(5)**, e0127174 (2015), doi:10.1371/journal.pone.0127174.
2. Gorska, M. *et al.* Neuronal nitric oxide synthase-mediated genotoxicity of 2-methoxyestradiol in hippocampal HT22 cell line. *Mol Neurobiol* (2015), doi: 10.1007/s12035-015-9434-5.
3. Kitao, H. *et al.* The antibodies against 5-bromo-2'-deoxyuridine specifically recognize trifluridine incorporated into DNA. *Sci Rep* **6(25286),** 1-12 (2016), doi: 10.1038/srep25286.
4. Strobel, B. *et al.* Riboswitch-mediated attenuation of transgene cytotoxicity increases adeno-associated virus vector yields in HEK-293 cells. *Am Soc Gene Cell Therapy* **23(10)**, 1582-1591 (2015), doi:10.1038/mt.2015.123.
5. Wu, Y. *et al.* The HepaRG cell line, a superior in vitro model to L-02, HepG2 and hiHeps cell lines for assessing drug-induced liver injury. *Cell Biol Toxicol* **32**, 37-59 (2016), doi:10.1007/s10565-016-9316-2.

Tropical disease

1. Ekins, S. *et al.* Machine learning models and pathway genome data base for *Trypanosoma cruzi* drug discovery. *PLOS Negl Trop Dis* **9(6)**, e0003878 (2015), doi: 10.1371/journal.pntd.0003878.
2. Prado, M. *et al.* Long-term live imaging reveals cytosolic immune responses of host hepatocytes against Plasmodium infection and parasite escape mechanisms. *Autophagy*, **11(9)**, 1561-1579 (2015), doi:10.1080/15548627.2015.1067361.

Virology

1. Calland, N. *et al.* Polyphenols inhibit Hepatitis C Virus entry by a new mechanism of action. *J Virol* **89(19)**, 10053-10063 (2015), doi: 10.1128/JVI.01473-15.
2. Furuyama, W. *et al.* Discovery of an antibody for pan-ebolavirus therapy. *Sci Rep* **6(20514)**, 1-10 (2016), doi: 10.1038/srep20514.
3. Galani, B. *et al.* Plant extracts from Cameroonian medicinal plants strongly inhibit hepatitis C virus infection *in vitro*. *Front Microbiol* **6(488)**, 1-9 (2015), doi: 10.3389/fmicb.2015.00488.
4. Kobayashi, S. *et al.* Rab8b regulates transport of West Nile Virus particles from recycling endosomes. *J Biol Chem* **291(12)**, 6659-6568 (2016), doi:10.1074/jbc.M115.712760.
5. Wood, E. *et al.* The role of phosphodiesterase 12 (PDE12) as a negative regulator of the innate immune response and the discovery of antiviral inhibitors. *J Biol Chem* **290(32)**, 19681-19696 (2015), doi: 10.1074/jbc.M115.653113.



Science: Researchers identify a novel antibody that shows promise in treating ebolavirus of all major species. Here, in a focus forming assay, they examine the effectiveness of their antibody in neutralizing a variety of ebolaviruses by incubating the purified antibody with infectious ebolaviruses. This study advances treatment of Ebola.

Technology: IN Cell Analyzer 2000 was used to count GFP-positive cells 20 hours after inoculation with the viruses in Vero E6 cells in order to calculate the percentage of infectivity.

Title: Discovery of an antibody for pan-ebolavirus therapy

Authors: W. Furuyama, A. Marzi, A. Nanbo, E. Haddock, J. Maruyama, H. Miyamoto, M. Igarashi, R. Yoshida, O. Noyori, H. Feldmann, A. Takada

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