

Stanford



Ramasamy Paulmurugan

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CONTACT INFORMATION

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Bio

ACADEMIC APPOINTMENTS

- Professor (Research), Radiology - Rad/Molecular Imaging Program at Stanford
- Member, Bio-X
- Member, Stanford Cancer Institute
- Member, Wu Tsai Neurosciences Institute

Teaching

COURSES

2023-24

- Current Topics in Applied Medicine: MED 211 (Aut)

2022-23

- Current Topics in Applied Medicine: MED 211 (Aut)

STANFORD ADVISEES

Postdoctoral Faculty Sponsor

Mahsa Bataghva Shahbaz, Wei Chen Lo, Sourabh Mehta, Farbod Tabesh, Suresh Thangudu

Publications

PUBLICATIONS

- Corrigendum to 'Molecular Identity Changes of Tumor-Associated Macrophages and Microglia After Magnetic Resonance Imaging-Guided Focused Ultrasound-Induced Blood-Brain Barrier Opening in a Mouse Glioblastoma Model' [Ultrasound in Med & Biol. 49 (2023) 1082-1090]. *Ultrasound in medicine & biology*
Zhang, Y., Wang, J., Ghobadi, S. N., Zhou, H., Huang, A., Gerosa, M., Hou, Q., Keunen, O., Golebiewska, A., Habte, F. G., Grant, G. A., Paulmurugan, R., Lee, et al
2023

- **Single-chain multicolor-reporter templates for subcellular localization of molecular events in mammalian cells.** *RSC chemical biology*
Kim, S. B., Paulmurugan, R., Kitada, N., Maki, S. A.
2023; 4 (12): 1043-1049
- **Protocol for in vitro sonoporation validation using non-targeted microbubbles for human studies of ultrasound-mediated gene delivery.** *STAR protocols*
Zhang, N., Guo, Y., Foiret, J., Tumbale, S. K., Paulmurugan, R., Ferrara, K. W.
2023; 4 (4): 102723
- **Single-chain multicolor-reporter templates for subcellular localization of molecular events in mammalian cells** *RSC CHEMICAL BIOLOGY*
Kim, S., Paulmurugan, R., Kitada, N., Maki, S. A.
2023
- **Correction to "Tumor Cell-Derived Extracellular Vesicle-Coated Nanocarriers: An Efficient Theranostic Platform for the Cancer-Specific Delivery of Anti-miR-21 and Imaging Agents".** *ACS nano*
Bose, R. J., Kumar, S. U., Zeng, Y., Afjei, R., Robinson, E., Lau, K., Bermudez, A., Habte, F., Pitteri, S. J., Sinclair, R., Willmann, J. K., Massoud, T. F., Gambhir, et al
2023
- **Correction to "SP94-Targeted Triblock Copolymer Nanoparticle Delivers Thymidine Kinase-p53-Nitroreductase Triple Therapeutic Gene and Restores Anticancer Function against Hepatocellular Carcinoma in Vivo".** *ACS applied materials & interfaces*
Sukumar, U. K., Rajendran, J. C., Gambhir, S. S., Massoud, T. F., Paulmurugan, R.
2023
- **Gold-Nanostar-Chitosan-Mediated Delivery of SARS-CoV-2 DNA Vaccine for Respiratory Mucosal Immunization: Development and Proof-of-Principle (vol 15, pg 17582, 2021)** *ACS NANO*
Kumar, U. S., Afjei, R., Ferrara, K., Massoud, T. F., Paulmurugan, R.
2023
- **Immune cell identity behind the Ktrans mapping of mouse glioblastoma.** *Magnetic resonance imaging*
Zhang, Y., Keunen, O., Golebiewska, A., Gerosa, M., Wang, J., Ghobadi, S. N., Huang, A., Hou, Q., Habte, F. G., Li, N., Grant, G., Paulmurugan, R., Lee, et al
2023
- **Enkurin: A novel marker for myeloproliferative neoplasms from platelet, megakaryocyte, and whole blood specimens.** *Blood advances*
Mosale Seetharam, S., Liu, Y., Wu, J., Fechter, L., Murugesan, K., Maecker, H. T., Gotlib, J., Zehnder, J. L., Paulmurugan, R., Krishnan, A.
2023
- **Synthesis and Evaluation of Clinically Translatable Targeted Microbubbles Using a Microfluidic Device for In Vivo Ultrasound Molecular Imaging.** *International journal of molecular sciences*
Bam, R., Natarajan, A., Tabesh, F., Paulmurugan, R., Dahl, J. J.
2023; 24 (10)
- **Bright Molecular Strain Probe Templates for Reporting Protein-Protein Interactions.** *Sensors (Basel, Switzerland)*
Kim, S. B., Furuta, T., Kamiya, G., Kitada, N., Paulmurugan, R., Maki, S. A.
2023; 23 (7)
- **New Frontiers in Three-Dimensional Culture Platforms to Improve Diabetes Research.** *Pharmaceutics*
Mohandas, S., Gayatri, V., Kumaran, K., Gopinath, V., Paulmurugan, R., Ramkumar, K. M.
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- **Modulation of Macrophages by In Situ Ligand Bridging** *ADVANCED FUNCTIONAL MATERIALS*
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- **Molecular Identity Changes of Tumor-Associated Macrophages and Microglia After Magnetic Resonance Imaging-Guided Focused Ultrasound-Induced Blood-Brain Barrier Opening in a Mouse Glioblastoma Model.** *Ultrasound in medicine & biology*
Zhang, Y., Wang, J., Ghobadi, S. N., Zhou, H., Huang, A., Gerosa, M., Hou, Q., Keunen, O., Golebiewska, A., Habte, F. G., Grant, G. A., Paulmurugan, R., Lee, et al
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- **Ligand Coupling and Decoupling Modulates Stem Cell Fate** *ADVANCED FUNCTIONAL MATERIALS*
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- **Enkurin: A novel marker for myeloproliferative neoplasms from platelet, megakaryocyte, and whole blood specimens.** *bioRxiv : the preprint server for biology*
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2023
- **FOXAI/2 depletion drives global reprogramming of differentiation state and metabolism in a human liver cell line and inhibits differentiation of human stem cell-derived hepatic progenitor cells.** *FASEB journal : official publication of the Federation of American Societies for Experimental Biology*
Warren, I., Moeller, M. M., Guiggey, D., Chiang, A., Maloy, M., Ogoke, O., Groth, T., Mon, T., Meamardoost, S., Liu, X., Thompson, S., Szeplowski, A., Thompson, et al
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- **Quantitative methods for molecular ultrasound imaging**
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- **3117- ENKURIN: A NOVEL MARKER FOR MYELOPROLIFERATIVE NEOPLASMS FROM VALIDATED PLATELET, MEGAKARYOCYTE, AND WHOLE BLOOD SPECIMENS (vol 111, pg S103, 2022)** *EXPERIMENTAL HEMATOLOGY*
Seetharam, S., Liu, Y., Wu, J., Fechter, L., Murugesan, K., Gotlib, J., Zehnder, J., Paulmurugan, R., Krishnan, A.
2023; 117: 69
- **Near-Infrared Imaging of Steroid Hormone Activities Using Bright BRET Templates.** *International journal of molecular sciences*
Kim, S., Nishihara, R., Paulmurugan, R.
2022; 24 (1)
- **Correction: Immunotheranostic microbubbles (iMBs) - a modular platform for dendritic cell vaccine delivery applied to breast cancer immunotherapy.** *Journal of experimental & clinical cancer research : CR*
Jugniot, N., Dahl, J. J., Paulmurugan, R.
2022; 41 (1): 357
- **Multimodal In Vivo Tracking of Chimeric Antigen Receptor T Cells in Preclinical Glioblastoma Models.** *Investigative radiology*
Wu, W. E., Chang, E., Jin, L., Liu, S., Huang, C., Kamal, R., Liang, T., Aissaoui, N. M., Theruvath, A. J., Pisani, L., Moseley, M., Stoyanova, T., Paulmurugan, et al
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- **A New Nrf2 Inhibitor Enhances Chemotherapeutic Effects in Glioblastoma Cells Carrying p53 Mutations.** *Cancers*
Afjei, R., Sadeghipour, N., Kumar, S. U., Pandrala, M., Kumar, V., Malhotra, S. V., Massoud, T. F., Paulmurugan, R.
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- **Photoswitchable Microgel for Dynamic Macrophage Modulation.** *Advanced materials (Deerfield Beach, Fla.)*
Kim, Y., Thangam, R., Yoo, J., Heo, J., Park, J. Y., Kang, N., Lee, S., Yoon, J., Mun, K. R., Kang, M., Min, S., Kim, S. Y., Son, et al
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- **Immunotheranostic microbubbles (iMBs) - a modular platform for dendritic cell vaccine delivery applied to breast cancer immunotherapy.** *Journal of experimental & clinical cancer research : CR*
Jugniot, N., Dahl, J. J., Paulmurugan, R.
2022; 41 (1): 299
- **Large-Scale Functionalized Metasurface-Based SARS-CoV-2 Detection and Quantification.** *ACS nano*
Ahmed, R., Guimaraes, C. F., Wang, J., Soto, F., Karim, A. H., Zhang, Z., Reis, R. L., Akin, D., Paulmurugan, R., Demirci, U.
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- **Evaluation of Immune Evasion in SARS-CoV-2 Delta and Omicron variants.** *Computational and structural biotechnology journal*
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- **Inhaled Gold Nano-star Carriers for Targeted Delivery of Triple Suicide Gene Therapy and Therapeutic MicroRNAs to Lung Metastases: Development and Validation in a Small Animal Model.** *Advanced therapeutics*
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- **Inhaled Gold Nano-Star Carriers for Targeted Delivery of Triple Suicide Gene Therapy and Therapeutic MicroRNAs to Lung Metastases: Development and Validation in a Small Animal Model** *ADVANCED THERAPEUTICS*
Liu, Y., Sukumar, U., Jugniot, N., Seetharam, S., Rengaramachandran, A., Sadeghipour, N., Mukherjee, P., Krishnan, A., Massoud, T. F., Paulmurugan, R.
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- **CD3 and CD8 targeting of ionizable lipid nanoparticles for in vivo mRNA delivery to T cells.**
Robinson, E. R., Kare, A. J., Kheirloom, A., Inayathullah, M., Tumbale, S. K., Wu, B., Raie, M. N., Seo, J. W., Salazar, F. B., Paulmurugan, R., Wu, A. M., Ferrara, K. W.
AMER ASSOC CANCER RESEARCH.2022
- **CD3 and CD8 targeting of ionizable lipid nanoparticles for in vivo mRNA delivery to T cells**
Robinson, E. R., Kare, A. J., Kheirloom, A., Inayathullah, M., Tumbale, S. K., Wu, B., Raie, M. N., Seo, J. W., Salazar, F. B., Paulmurugan, R., Wu, A. M., Ferrara, K. W.
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- **Biomimetic nanobubbles for triple-negative breast cancer targeted ultrasound molecular imaging.** *Journal of nanobiotechnology*
Jugniot, N., Massoud, T. F., Dahl, J. J., Paulmurugan, R.
2022; 20 (1): 267
- **Correction to: The protean world of non-coding RNAs in glioblastoma.** *Journal of molecular medicine (Berlin, Germany)*
Paulmurugan, R., Malhotra, M., Massoud, Z. T., Massoud, T. F.
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Kar, S., Jaswandkar, S. V., Katti, K. S., Kang, J. W., So, P. T., Paulmurugan, R., Liepmann, D., Venkatesan, R., Katti, D. R.
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- **Submolecular Tuning of Ligand Size and Spacing for Dynamic Macrophage Modulation.** *Advanced materials (Deerfield Beach, Fla.)*
Kim, Y., Koo, T. M., Thangam, R., Kim, M. S., Jang, W. Y., Kang, N., Min, S., Kim, S. Y., Yang, L., Hong, H., Jung, H. J., Koh, E. K., Patel, et al
2022: e2110340
- **FN3 linked nanobubbles as a targeted contrast agent for US imaging of cancer-associated human PD-L1.** *Journal of controlled release : official journal of the Controlled Release Society*
Kumar, U. S., Natarajan, A., Massoud, T. F., Paulmurugan, R.
2022
- **Receptor-Level Proximity and Fastening of Ligands Modulates Stem Cell Differentiation** *ADVANCED FUNCTIONAL MATERIALS*
Bae, G., Kim, M., Thangam, R., Koo, T., Jang, W., Yoon, J., Han, S., Yang, L., Kim, S., Kang, N., Min, S., Hong, H., Fu, et al
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- **Local Sound Speed Estimation for Pulse-Echo Ultrasound in Layered Media** *IEEE TRANSACTIONS ON ULTRASONICS FERROELECTRICS AND FREQUENCY CONTROL*
Ali, R., Telichko, A., Wang, H., Sukumar, U. K., Vilches-Moure, J. G., Paulmurugan, R., Dahl, J. J.
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- **Contrast Enhanced Ultrasound Molecular Imaging of Spontaneous Chronic Inflammatory Bowel Disease in an Interleukin-2 Receptor alpha-/- Transgenic Mouse Model Using Targeted Microbubbles.** *Nanomaterials (Basel, Switzerland)*
Wang, H., Vilches-Moure, J. G., Bettinger, T., Cherkaoui, S., Lutz, A., Paulmurugan, R.
1800; 12 (2)
- **Ultrasound-Guided Microbubble-Mediated Locoregional Delivery of Multiple MicroRNAs Improves Chemotherapy in Hepatocellular Carcinoma.** *Nanotheranostics*
Wang, H., Hu, Z., Sukumar, U. K., Bose, R. J., Telichko, A., Dahl, J. J., Paulmurugan, R.
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- **Manipulating Nanoparticle Aggregates Regulates Receptor-Ligand Binding in Macrophages.** *Journal of the American Chemical Society*
Kim, Y., Jung, H. J., Lee, Y., Koo, S., Thangam, R., Jang, W. Y., Kim, S. Y., Park, S., Lee, S., Bae, G., Patel, K. D., Wei, Q., Lee, et al
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- **ENKURIN: A NOVEL MARKER FOR MYELOPROLIFERATIVE NEOPLASMS FROM VALIDATED PLATELET, MEGAKARYOCYTE, AND WHOLE BLOOD SPECIMENS**
Krishnan, A., Seetharam, S., Liu, Y., Wu, J., Fechter, L., Murugesan, K., Gotlib, J., Zehnder, J., Paulmurugan, R.
ELSEVIER SCIENCE INC.2022: S103
- **One-Channel Microsliding Luminometer for Quantifying Low-Energy Bioluminescent Lights.** *Methods in molecular biology (Clifton, N.J.)*
Kim, S., Paulmurugan, R.
2022; 2525: 365-375
- **Quantitative Imaging of Retinoic Acid Activities in Living Mammalian Cells.** *Methods in molecular biology (Clifton, N.J.)*
Kim, S., Fujii, R., Paulmurugan, R.
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- **Compact Eight-Channel Light-Sensing System for Bioassays.** *Methods in molecular biology (Clifton, N.J.)*
Kim, S., Hori, S. S., Sadeghipour, N., Sukumar, U. K., Paulmurugan, R.
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- **BRET Sensors for Imaging Membrane Integrity of Microfluidically Generated Extracellular Vesicles.** *Methods in molecular biology (Clifton, N.J.)*
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- **Editorial: Nanomaterials for targeted delivery of therapeutic and imaging agents.** *Frontiers in cell and developmental biology*
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2022; 10: 978690
- **Noninvasive estimation of local speed of sound by pulse-echo ultrasound in a rat model of nonalcoholic fatty liver.** *Physics in medicine and biology*
Telichko, A. V., Ali, R., Brevett, T., Wang, H., Vilches-Moure, J., Kumar, S. U., Paulmurugan, R., Dahl, J. J.
1800
- **Engineered Cell-Derived Vesicles Displaying Targeting Peptide and Functionalized with Nanocarriers for Therapeutic microRNA Delivery to Triple-Negative Breast Cancer in Mice.** *Advanced healthcare materials*
Bose, R. J., Kumar, U. S., Garcia-Marques, F., Zeng, Y., Habte, F., McCarthy, J. R., Pitteri, S., Massoud, T. F., Paulmurugan, R.
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- **Expression and purification of a native Thy1-single-chain variable fragment for use in molecular imaging.** *Scientific reports*
Jugniot, N., Bam, R., Paulmurugan, R.
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- **Detection and Characterization of Sentinel Lymph Node by Ultrasound Molecular Imaging with B7-H3-Targeted Microbubbles in Orthotopic Breast Cancer Model in Mice.** *Molecular imaging and biology*
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Kumar, U. S., Afjei, R., Ferrara, K., Massoud, T. F., Paulmurugan, R.
2021
- **Dynamic Ligand Screening by Magnetic Nanoassembly Modulates Stem Cell Differentiation.** *Advanced materials (Deerfield Beach, Fla.)*
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- **Camouflaged Hybrid Cancer Cell-Platelet Fusion Membrane Nanovesicles Deliver Therapeutic MicroRNAs to Presensitize Triple-Negative Breast Cancer to Doxorubicin.** *Advanced functional materials*
Liu, Y., Sukumar, U. K., Kanada, M., Krishnan, A., Massoud, T. F., Paulmurugan, R.
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- **Magnetic Control and Real-Time Monitoring of Stem Cell Differentiation by the Ligand Nanoassembly.** *Small (Weinheim an der Bergstrasse, Germany)*
Lee, S., Kim, M. S., Patel, K. D., Choi, H., Thangam, R., Yoon, J., Koo, T. M., Jung, H. J., Min, S., Bae, G., Kim, Y., Han, S., Kang, et al
2021; e2102892
- **Advances in Engineered Polymer Nanoparticle Tracking Platforms towards Cancer Immunotherapy-Current Status and Future Perspectives.** *Vaccines*
Thangam, R., Patel, K. D., Kang, H., Paulmurugan, R.
2021; 9 (8)
- **Camouflaged Hybrid Cancer Cell-Platelet Fusion Membrane Nanovesicles Deliver Therapeutic MicroRNAs to Presensitize Triple-Negative Breast Cancer to Doxorubicin** *ADVANCED FUNCTIONAL MATERIALS*
Liu, Y., Sukumar, U. K., Kanada, M., Krishnan, A., Massoud, T. F., Paulmurugan, R.
2021
- **Immunoregulation of Macrophages by Controlling Winding and Unwinding of Nanohelical Ligands** *ADVANCED FUNCTIONAL MATERIALS*
Bae, G., Jeon, Y., Ko, M., Kim, Y., Han, S., Thangam, R., Kim, W., Jung, H., Lee, S., Choi, H., Min, S., Hong, H., Park, et al
2021
- **Management of COVID-19: Current Status and Future Prospects.** *Microbes and infection*
Kabir, M. A., Ahmed, R., Chowdhury, R., Asher Iqbal, S. M., Paulmurugan, R., Demirci, U., Asghar, W.
2021; 104832
- **Passive Cavitation Mapping by Cavitation Source Localization From Aperture-Domain Signals-Part II: Phantom and In Vivo Experiments** *IEEE TRANSACTIONS ON ULTRASONICS FERROELECTRICS AND FREQUENCY CONTROL*
Telichko, A., Lee, T., Hyun, D., Chowdhury, S., Bachawal, S., Herickhoff, C. D., Paulmurugan, R., Dahl, J. J.
2021; 68 (4): 1198–1212
- **Ultrasound Triggered Co-Delivery of Therapeutic MicroRNAs and a Triple Suicide Gene Therapy Vector by Using Biocompatible Polymer Nanoparticles for Improved Cancer Therapy in Mouse Models** *ADVANCED THERAPEUTICS*
Kumar, S., Wang, H., Telichko, A. V., Natarajan, A., Bettinger, T., Cherkaoui, S., Massoud, T. F., Dahl, J. J., Paulmurugan, R.
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- **Diagnosis For COVID-19: Current Status and Future Prospects.** *Expert review of molecular diagnostics*
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2021
- **Remote Switching of Elastic Movement of Decorated Ligand Nanostructures Controls the Adhesion-Regulated Polarization of Host Macrophages** *ADVANCED FUNCTIONAL MATERIALS*
Thangam, R., Kim, M., Bae, G., Kim, Y., Kang, N., Lee, S., Jung, H., Jang, J., Choi, H., Li, N., Kim, M., Park, S., Kim, et al
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- **Remote Control of Time-Regulated Stretching of Ligand-Presenting Nanocoils In Situ Regulates the Cyclic Adhesion and Differentiation of Stem Cells.** *Advanced materials (Deerfield Beach, Fla.)*
Min, S., Ko, M. J., Jung, H. J., Kim, W., Han, S., Kim, Y., Bae, G., Lee, S., Thangam, R., Choi, H., Li, N., Shin, J. E., Jeon, et al
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- **Ferroptosis inducers are a novel therapeutic approach for advanced prostate cancer.** *Cancer research*
Ghoochani, A. n., Hsu, E. C., Aslan, M. n., Rice, M. A., Nguyen, H. M., Brooks, J. D., Corey, E. n., Paulmurugan, R. n., Stoyanova, T. n.
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- **Ligand-Activatable BRET9 Probes for Imaging Molecular Events in Living Mammalian Cells.** *Methods in molecular biology (Clifton, N.J.)*
Kim, S., Fujii, R., Paulmurugan, R.
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- **Highly Bright NIR-BRET System for Imaging Molecular Events in Live Cells.** *Methods in molecular biology (Clifton, N.J.)*
Nishihara, R., Suzuki, K., Kim, S., Paulmurugan, R.
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- **High-Throughput Whole-Plate Imaging of Cells for Multiple Biological Applications.** *Methods in molecular biology (Clifton, N.J.)*
Sukumar, U. K., Habte, F., Massoud, T. F., Paulmurugan, R.
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- **Wearable Collector for Noninvasive Sampling of SARS-CoV-2 from Exhaled Breath for Rapid Detection.** *ACS applied materials & interfaces*
Soto, F., Ozen, M. O., Guimarães, C. F., Wang, J., Hokanson, K., Ahmed, R., Reis, R. L., Paulmurugan, R., Demirci, U.
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- **Minicircles for a two-step blood biomarker and PET imaging early cancer detection strategy.** *Journal of controlled release : official journal of the Controlled Release Society*
Robinson, E. R., Gowrishankar, G., D'Souza, A., Kheirolomoom, A., Haywood, T., Hori, S. S., Chuang, H. Y., Zeng, Y., Tumbale, S., Aalipour, A., Beinat, C., Alam, I. S., Sathirachinda, et al
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2021; 281: 121339
- **A Microfluidics-Based Scalable Approach to Generate Extracellular Vesicles with Enhanced Therapeutic MicroRNA Loading for Intranasal Delivery to Mouse Glioblastomas.** *ACS nano*
Wang, K., Kumar, U. S., Sadeghipour, N., Massoud, T. F., Paulmurugan, R.
2021
- **Functionalized Nanomaterials as Tailored Theranostic Agents in Brain Imaging.** *Nanomaterials (Basel, Switzerland)*
Thangam, R., Paulmurugan, R., Kang, H.
2021; 12 (1)
- **A Priori Activation of Apoptosis Pathways of Tumor (AAAPT) technology: Development of targeted apoptosis initiators for cancer treatment.** *PLoS one*
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- **Current status of targeted microbubbles in diagnostic molecular imaging of pancreatic cancer.** *Bioengineering & translational medicine*
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2021; 6 (1): e10183
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Peterson, K. M., Franchi, F. n., Olthoff, M. n., Paulmurugan, R. n., Rodriguez-Porcel, M. n.
2021; 1 (3): e62
- **Acoustically Driven Microbubbles Enable Targeted Delivery of microRNA-Loaded Nanoparticles to Spontaneous Hepatocellular Neoplasia in Canines.** *Advanced therapeutics*
Kumar, S. U., Telichko, A. V., Wang, H., Hyun, D., Johnson, E. G., Kent, M. S., Rebhun, R. B., Dahl, J. J., Culp, W. T., Paulmurugan, R.
2020; 3 (12)
- **Acoustically Driven Microbubbles Enable Targeted Delivery of microRNA-Loaded Nanoparticles to Spontaneous Hepatocellular Neoplasia in Canines** *ADVANCED THERAPEUTICS*
Kumar, S., Telichko, A. V., Wang, H., Hyun, D., Johnson, E. G., Kent, M. S., Rebhun, R. B., Dahl, J. J., Culp, W. N., Paulmurugan, R.
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- **Therapeutic Ultrasound Parameter Optimization for Drug Delivery Applied to a Murine Model of Hepatocellular Carcinoma.** *Ultrasound in medicine & biology*
Telichko, A. V., Wang, H., Bachawal, S., Kumar, S. U., Bose, J. C., Paulmurugan, R., Dahl, J. J.
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- **SARS-CoV-2 Vaccine Development: An Overview and Perspectives.** *ACS pharmacology & translational science*
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2020; 3 (5): 844–58
- **Bioluminescent Imaging Systems for Assay Developments.** *Analytical sciences : the international journal of the Japan Society for Analytical Chemistry*
Kim, S., Paulmurugan, R.
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