



ABOUT OUR LABORATORY

Projects are conducted by the **Controlled in vitro Microenvironments (CivM) Laboratory** at the Izmir Institute of Technology. Our long term goal is to better understand the cell biology of breast cancer metastasis. It is known that changes in three important biological processes namely, cell adhesion, matrix degradation and cell motility play crucial roles in metastasis. To achieve our goal, we focus on:

- Design and fabrication of micro- and nano-devices that mimic the cellular microenvironment
- Micro-environmental control and biophysics of cell adhesion, migration and invasion in breast cancer

We use tools of nanotechnology such as UV lithography and electron beam lithography to create *Controlled in vitro Microenvironments (CivM)*. CivM allows us to investigate the breast cancer microenvironment with precise control of spatial (2D and 3D; nanometers to centimeters) and temporal (seconds to days) parameters. Finally, we use various fluorescence microscopy techniques to examine the cell biology in CivM.

We intend to use CivM we develop for diagnostic purposes.



Curiosity

Creativity

Courage

Collaboration

PATENTS

Three Dimensional Microfluidic Device that Determines Metastatic Capacity and Homing Choices

- Publication Number: EP2741083
- Publication Date: 2014-06-11
- Inventor and Applicant: Devrim Pesen Okvur

Microfluidic Device for Investigation of Distance Dependent Interactions in Cell Biology (Patent Pending)

- Application Number: PCT/EP2014/070839
- Application Date: 2014-09-29
- Inventor and Applicant: Devrim Pesen Okvur

FOR MORE INFORMATION

Devrim Pesen Okvur, Ph.D.

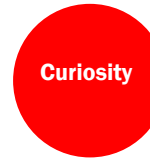
Controlled in vitro Microenvironments Laboratory

Address: Izmir Institute of Technology,
Gulbahce Campus, Faculty of Science Department of

MBG, Room D-106, 35430 Urla Izmir Turkey

Tel: + 90 232 750 7304 / 7347

Web: <http://web.iyte.edu.tr/~devrimpesen/>



SCIENCE AT



Distance Dependent Interactions: DDI-chip

Understanding Cellular Interactions in Health and Disease

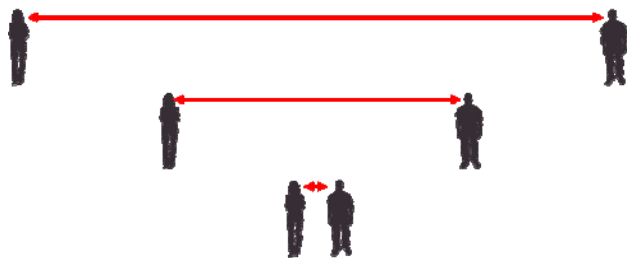
&

Metastatic Capacity and Homing Choices: MetaHoming-chip

Revolutionizing Cancer Diagnostics and Therapy

DEV R I M P E S E N O K V U R
P H . D .

Controlled *in vitro*
Microenvironments
Laboratory



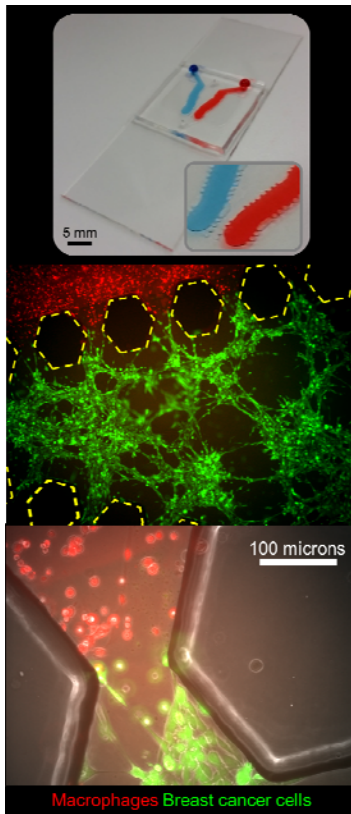
Distance Dependent Interactions: DDI-chip

Microfluidic technology enables realistic study of cells in both health and disease states, improving drug development, reducing animal testing, and significantly lowering research costs

Challenge: Medical and life sciences are in dire need of platforms that can truly mimic the physiological microenvironment: Despite of billions of dollars spent, less than 10% of clinical trials can provide promising results towards therapy.

Solution: The DDI-chip is a microfluidic device that positions cells and factors to be investigated at different distances from each other. This provides a more physiological setup and allows simultaneous investigation of different distances in one device. The DDI-chip also makes it possible to test agents that can affect distance dependent interactions.

In one application, one side channel can simulate a blood vessel and the other side channel can be embedded with cancer cells. The response of cancer cells as a function of their distance to a blood vessel can be investigated, with or without drugs.



Microfluidic device for investigation of distance dependent interactions in cell biology (PCT Patent PCT/EP2014/070839, September 2014)

The DDI-chip can also be used to investigate, e.g. autocrine signaling: Since the width of the central microfluidic channel increases along the DDI-chip, the number of cells in the central channel increases and so does any parameter that positively correlates with cell number.

Moreover, a blood vessel of increasing size can be simulated within the central channel of the DDI-chip. Here, changes in the flow of blood as well as drug delivery and/or extravasation of cancer cells to the nearby tissue simulated by the side channels can be investigated.

The magic of the DDI-chip is that it allows for investigation of many different types of interactions which are central to proper functioning of cells in our bodies. To enable efficient research that will provide cures for many different types of diseases from cancer to atherosclerosis, the DDI-Chip provides a low-cost and effective solution to the pharmaceutical industry, medical, and life sciences research.

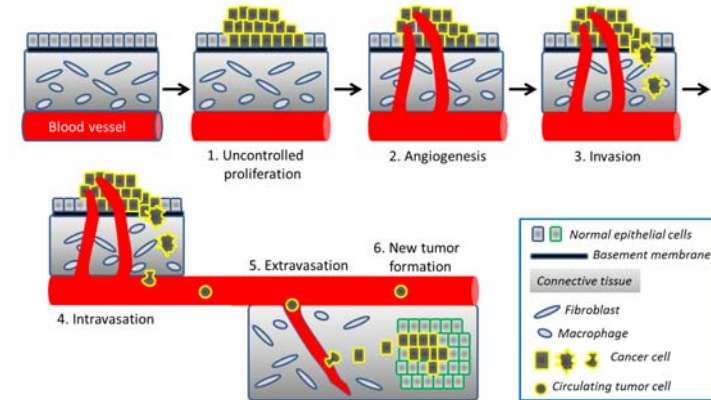


Metastatic Capacity and Homing Choices: MetaHomingChip

Will the tumor metastasize? To which organ will the tumor metastasize? There is a dire need to answer these questions both in the pharmaceutical industry and the healthcare sector.

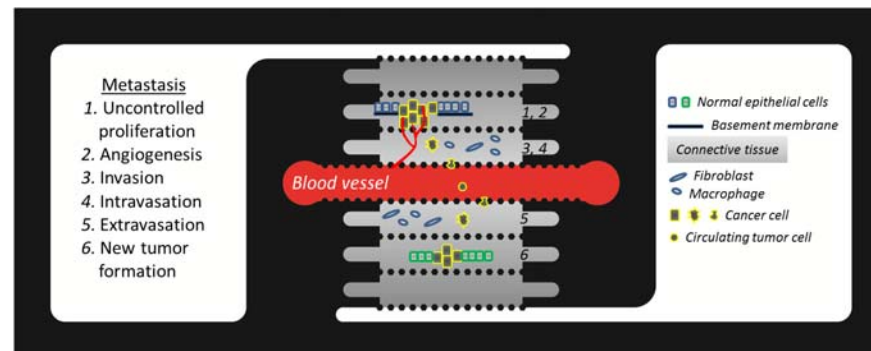
Challenge: The leading cause of death for cancer patients is metastasis. Even if the primary tumor is surgically removed, cells that could have spread from the primary tumor can cause formation of new tumors and recurrence of cancer. There is no test that can show whether cancer will recur or not or which type of tissue cancer cells will prefer for possible new tumor sites.

Solution: The MetaHomingChip is a microfluidic device that determines metastatic capacity and homing choices. The device mimics the *in vivo* tumor microenvironment comprising different cell types, matrices, biological molecules and chemicals. All steps of metastasis, namely, angiogenesis, matrix invasion, cell migration, intravasation, circulation, extravasation and new tumor formation, can be simultaneously and jointly investigated using MetaHomingChip. In addition, the chip allows testing of the effectiveness and specificity of anti-metastatic drugs.



Furthermore, cancer cells are known to prefer certain sites in the body to form secondary tumors. The answer to 'where tumor cells metastasize to' have prognostic value. For example, breast cancer metastasizing to the lungs has a poorer prognosis than that metastasizing to the bone. Therefore, determining the homing choices will help select the best course of treatment and enable personalized medicine.

Watch out: MetaHoming Chip is about to revolutionize cancer diagnostics and therapy.



Three dimensional microfluidic device that determines metastatic capacity and homing choices (EPO Patent EP13154001.5, February 2013)



ATMOSFER TTO

TECHNOLOGY TRANSFER SERVICES

- Commercialization consultancy for international patent and licensing
- Proposal and consortium support for European Commission grants (e.g, H2020, ERC, etc)
- Incubation programs and entrepreneur promotion
- Connect international research experts, entrepreneurs, and investors to people just like you!



atmosfer@atmosfertto.com



+90 232 502 0018

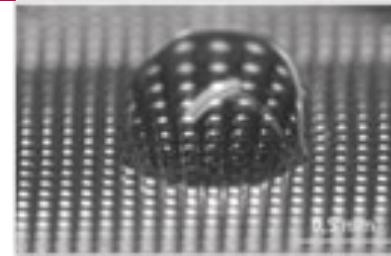
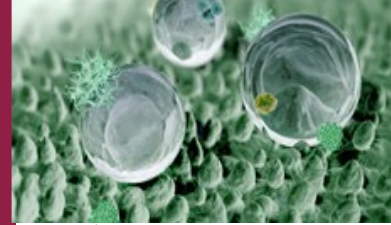


Atmosfer Teknoloji Transfer Ofisi (TTO)
İYTE Kampüsü Teknopark A1 Blok No:1
35430 Urla-İZMİR, TÜRKİYE

www.atmosfertto.com

İYTE

Nano-
Technology
at İzmir
Institute of
Technology



ATMOSFER TTO

Izmir Institute of Technology

Technology Transfer Office (TTO)



**INNOVATIVE
RESEARCH
FROM A EURASIA
PARTNER!**



- Founded in 1992 as a state university and is the only “Turkish” Institute of Technology
- Focus is on education and research across three major faculties: science, engineering, and architecture
- Language of instruction is English
- Several international students from more than 40 different countries
- Active member of the European Community Action Scheme for the Mobility of University Students (ERASMUS) exchange program
- Largest campus in Izmir with over 3,500 hectares campus area



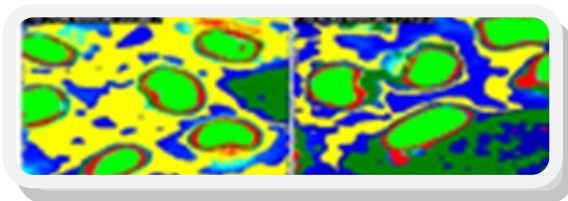
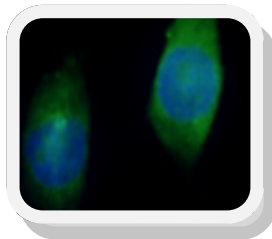
DR. VOLGA BULMUS

Professor, Bioengineering
Macromolecular Engineering

Specialties: Nano-medicine, Polymer Therapeutics, Functional Polymers, Polymer Synthesis, Drug Delivery

Applications: Biological Sciences, Chemistry, Health, Medical, Materials

- Synthesized new biosynthetic hybrid polymers that potentially enhance cytosolic delivery of therapeutic agents.
- Consulting expertise in intracellular drug delivery, polymeric drug delivery, polymer therapeutics, polymer nanomedicines, polymeric nanoparticles, functional polymers, polymer chemistry, RAFT polymerization



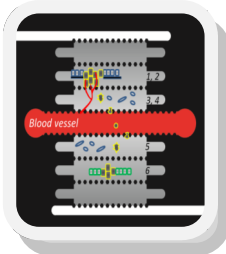
DR. DEVRIM PESEN OKVUR

Associate Professor, Molecular Biology & Genetics
Controlled *in vitro* Microenvironments Laboratory

Specialties: Microfluidics for 3D cell culture, micro/nano 2D/3D patterning (UV and electron beam lithography), cancer cell biology

Applications: Biological Sciences, Health, Medical

- Investigated “Interactions of Breast Cancer Cells with Macrophages in Controlled 3D *in vitro* Microenvironments,” “Adhesion at the Nanometer Scale: Breast Cancer Cells and Normal Epithelial Cells,” and “Invadopodia Formation on Nanometer Scale Protein Patterns”.
- Consulting expertise in cancer microenvironment, microfluidics for 3D cell culture, UV lithography, electron beam lithography
- Currently seeking licensor for two patented microfluidic devices:



1.DDI-Chip: Low cost and effective solution to investigate distance dependent cell interactions and test agents (PCT Patent PCT/EP2014/ 070839, Sept2014)

2.MetaHomingChip: Three dimensional microfluidic device that determines metastatic capacity and homing choices that will revolutionize cancer diagnostics (EPO Patent EP13154001.5, Feb2013)

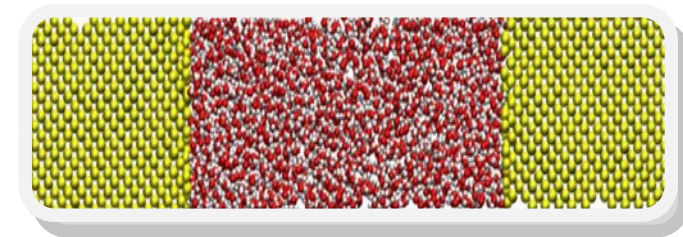
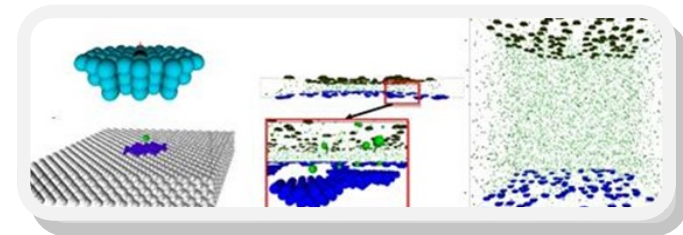
DR. MURAT BARISIK

Assistant Professor, Mechanical Engineering
Micro/Nano Engineering Group

Specialties: Micro/Nanoflows, Microfluidics, Heat Transport, Electrokinetic Phenomena

Applications: Mechanical Engineering, Aerospace & Defense, Physics, Energy

- Examined surface effects on nano gas/liquid flows, interface thermal resistance in nano heat transfer and nano-size effects on nanoparticle surface charging and transport.
- Selected by the European Union Marie Skłodowska-Curie COFUND to explore “Molecular Level Investigation of Nano-Scale Gas Flows”
- Consulting expertise in molecular modeling, heat transfer and fluid flow



Medical and life sciences are in dire need of platforms that can truly mimic the physiologic microenvironment: Despite of billions of dollars spent, less than 10% of clinical trials can provide promising results towards cancer therapy.

Microfluidic technology provides precise spatial and temporal control, high-throughput analysis, low fabrication costs and portability. Material consumption and waste volumes can be as low as picoliters. Using small volumes of unknown or toxic materials provides safe experimental study. Moreover, microfluidic technology can provide means to mimic physiological microenvironments. This feature can help us more realistically study cells in both health and disease states and thus improve drug development. Finally, microfluidic technology can help reduce animal testing. It is no surprise that the microfluidic technology market is worth billions of dollars with a continuous and better than estimated rise.

Interactions of cells with factors such as same or different types of cells, soluble factors or matrix bound soluble factors, depend on the distances between cells and the factors. For example, macrophage cells of the immune system can be lured by breast cancer cells that express a certain growth factor. Here, immune system cells that are supposed to work against cancer cells end up helping them. Different cells can show different interaction mechanisms such as autocrine, juxtacrine, paracrine, endocrine signaling. Cells can give chemotactic, haptotactic, durotactic responses to different factors. Research in cancer, stem cells, immunology, development, endocrinology, neuroscience etc. require better devices that can investigate interactions of cells with factors such as those mentioned above.

The invention presented here, the DDI-chip (Distance Dependent Interactions-chip) is a microfluidic device. The DDI-chip positions the cells and factors to be investigated at different distances from each other and thus provides a more physiological setup. In addition, the DDI-chip allows simultaneous investigation of different distances in one device. The DDI-chip also makes it possible to test agents that can affect distance dependent interactions. In one application, one of the side channels can simulate a blood vessel and the other side channel can be embedded with cancer cells. Thus response of cancer cells as a function of their distance to a blood vessel with or without drugs can be investigated. The DDI-chip can also be used to investigate, e.g. autocrine signaling: Since the width of the central microfluidic channel increases along the DDI-chip, the number of cells in the central channel increases and thus any parameter that positively correlates with cell number will also increase. Moreover, a blood vessel of increasing width can be simulated within the central channel of the DDI-chip. Here, changes in the flow of blood as well as drug delivery and/or extravasation of cancer cells to the neighboring tissue simulated by the side channels can be investigated.

The magic of the DDI-chip is that it allows for investigation of many different types of interactions which are central to proper functioning of cells in our bodies. To enable efficient research that will provide cures for many different types of diseases from cancer to atherosclerosis, we sure can take advantage of the DDI-chip.

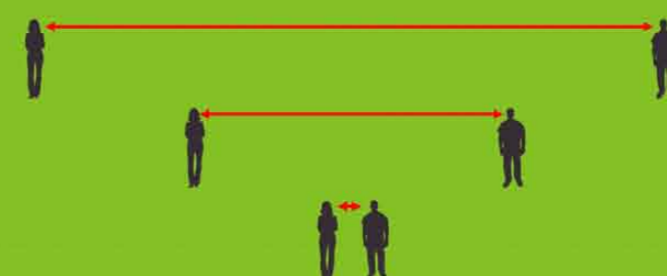
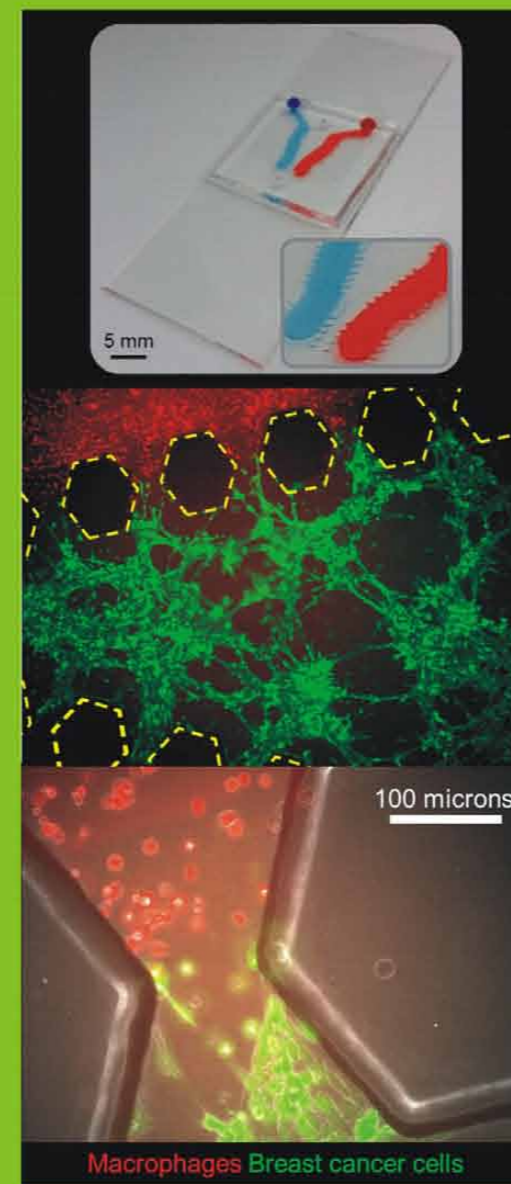
Les sciences médicales et de la vie ont un besoin urgent de plates-formes qui peuvent vraiment imiter le microenvironnement physiologique: Malgré des milliards de dollars dépensés, moins de 10% des essais cliniques peut donner des résultats prometteurs pour la thérapie du cancer.

La technologie micro fluidique permet d'effectuer un contrôle précis spatial et temporel, une analyse à haut débit, les coûts de fabrication faibles et la portabilité. Les volumes de consommation et de déchets peuvent être aussi bas que picolitres. L'utilisation de petits volumes de matériaux inconnus ou toxiques fournit étude expérimentale de sécurité. En outre, la technologie micro fluidique peut fournir des moyens pour imiter des microenvironnements physiologiques. Cette fonctionnalité peut nous aider à étudier de façon plus réaliste à la fois de pour santé et pour l'état de maladie et d'améliorer ainsi le développement de médicaments. Enfin, la technologie micro fluidique peut aider à réduire l'expérimentation animale. Il n'est pas surprenant que le marché de la technologie micro fluidique vaut des milliards de dollars avec un rythme continu et plus que la hausse estimée.

Les interactions de cellules avec des facteurs de types identiques ou différents de cellules, la matrice des facteurs solubles ou liés aux facteurs solubles, dépendent des distances entre les cellules et les facteurs. Par exemple, les cellules macrophages du système immunitaire peuvent être attirées par les cellules cancéreuses du sein qui expriment un certain facteur de croissance. Ici, les cellules du système immunitaire qui sont censés travailler contre les cellules cancéreuses finissent par les aider. Les différentes cellules peuvent montrer de différents mécanismes d'interaction tels qu'autocrine, juxtacrine, paracrine, signalisation endocrinien. Les cellules peuvent donner des réponses chimiotactique, Duro tactiques, haptotactiques aux différents facteurs. La recherche sur le cancer, les cellules souches, l'immunologie, le développement, l'endocrinologie, les neurosciences, etc. exigent de meilleurs dispositifs qui peuvent étudier les interactions de cellules avec des facteurs tels que ceux mentionnés ci-dessus.

L'invention présentée ici, la puce DDI (Interactions dépendantes de Distance - Puce) est un dispositif micro fluidique. La puce DDI positionne les cellules et les facteurs à examiner à des distances différentes de l'un à l'autre et fournit ainsi une configuration plus physiologique. En outre, la puce DDI permet d'étudier de manière simultanée, de différentes distances en un seul appareil. La puce DDI permet également de tester des agents qui peuvent affecter les interactions dépendantes de distance. Dans une application, une des chaînes latérales peut simuler un vaisseau sanguin et l'autre chaîne latérale peut être intégrée avec les cellules cancéreuses. Ainsi, la réponse des cellules cancéreuses en fonction de leur distance par rapport à un vaisseau sanguin, avec ou sans médicaments peut être étudiée. La puce DDI peut également être utilisée pour étudier, par exemple, la signalisation autocrine: Comme la largeur des canaux micro fluidiques centraux augmente le long de la puce DDI, le nombre de cellules dans le canal central augmente ainsi et un paramètre quelconque qui est en corrélation positive avec le nombre de cellules augmente également. En outre, un vaisseau sanguin de largeur croissante peut être simulé à l'intérieur du canal central de la puce DDI. Ici, les changements dans la circulation du sang ainsi que l'administration de médicaments et / ou de l'extravasation des cellules cancéreuses aux tissus voisins simulée par les chaînes latérales peuvent être étudiés.

La magie de la puce DDI est qu'elle permet d'enquêter sur les nombreux différents types d'interactions qui sont au cœur de bon fonctionnement des cellules de notre corps. Pour permettre une recherche efficace qui fournira des traitements pour de nombreux types de maladies de cancer athéroscléroses, nous pouvons profiter de la puce DDI.



Inventor / Inventeur	:Devrim PESEN OKVUR
Telephone / Téléphone	:+90 232 750 73 04 / +90 538 868 84 41
E-mail	:devrimpesenokvur@gmail.com devrimpesen@iyte.edu.tr

“Meet the wind of mind”

PRODUCE WITH MIND
PROFIT WITH REGISTRY

TURKISH PATENT INSTITUTE

Hipodrom Cad. No: 115
06330 Yenimahalle/ANKARA/TURKEY
Tel: (+90 312) 3031000
Faks: (+90 312) 3031173
www.turkpatent.gov.tr
info@tpe.gov.tr





TECHNOLOGY PROJECTS & TRENDS

USING MICROFLUIDICS TO DIAGNOSE CANCER AND UNDERSTAND CELLULAR INTERACTIONS



DR. DEVRİM PESEN OKVUR

Associate Professor, Molecular Biology & Genetics

Controlled *in vitro* Microenvironments Laboratory

cells and then began to perform research in nanotechnology such as patterning proteins at the nanometer scales and I was hooked. I saw a lot of potential with the tools in nanotechnology for cell biology since cells and proteins are at the nano and micro meter scale and you need tools that give you control at these scales.

What do you concentrate on in Controlled *in vitro* Microenvironments Laboratory?

We attempt to understand how cancer cells behave compared to normal cells and understand features specific to the cancer cell. Three things that go wrong in cancer are adhesion, migration, and invasion. So we try to understand these events, what goes wrong, and how we can better characterize them.

How did you get started in interdisciplinary research?

I received my Bachelor's from Bilkent and then my PhD from Johns Hopkins. At that time, molecular biology was a very hot topic and I needed to set myself apart because all these people were going to know the same things as me when we graduate. How can I compete? So after my PhD, I knew I had to have an "edge" to make me more competitive for the positions.

I also have interests in several different things. If you want to do something new, you have to learn more than one thing. (*Eg if you keep being a biologist all the time, you will keep doing things the same way because you will always look from the same angle*).

I began working on the mechanical properties of

ATMOSFER SUPPORT

- Promotional Materials and Brochure Support
- Coaching Service
- Patent Valuation and Commercialization Support

Dr. Devrim Pesen Okvur is currently seeking a licensor for two patented microfluidic devices:

- DDI-Chip: Low cost and effective solution to investigate distance dependent cell interactions and test agents (PCT Patent PCT/EP2014/ 070839, Sept2014)
- MetaHomingChip: Three dimensional microfluidic device that determines metastatic capacity and homing choices that will revolutionize cancer diagnostics (EPO Patent EP13154001.5, Feb2013)



What are your most recent accomplishments?

Two major inventions so far and more coming... we filed two patents for cancer cell biology, the first is about interactions between cells and cellular communication, there are different communication mechanisms based on distances. Like people, cells communicate differently depending on the distance between them and their health. In sickness, communication may be disturbed or interrupted. Most of the drugs we try to develop are trying to restore this communication. The main use for the DDI chip is to accelerate drug discovery using micro-fluidics. This product is ready to sell.

In my lab, we are creating micro-environments by controlling space and time using micro-nano scale. "

For the second one, we are focusing on metastasis and homing choices to determine the prognosis. I am hoping to license or work with drug companies to finalize the product.

Our TÜBİTAK 1003 collaboration project titled "Drug Delivery via Targeted Microbubbles as Ultrasound Contrast Agent and Their Use in Cancer Treatment via Controlled Local Drug Release" is ongoing. My lab carries out CivM experiments with principal investigator Dr. Sevgi Kılıç Özdemir from the Department of Chemical Engineering at IYTE and in collaboration with Dr. Mustafa Seçil from the Department of Radiology, School of Medicine at Dokuz Eylül University.

Most recently, I was selected by **Turkish Patent Institute** to represent Turkey at the **43rd International Exhibition of Inventions** in Geneva. My invention was awarded a gold medal by the international jury in the in the medical category (Medicine-Surgery-Hygiene-Orthopedics).

Finally, our paper titled "Differentiation of Normal and Cancer Cell Adhesion on Custom Designed Protein Nanopatterns" was recently accepted by ACS Nano Letters, a leading journal in the field.

So what's next?

In my new TÜBİTAK 1001 project to start this October, my lab will develop a 3D in vitro model to study new tumor formation following extravasation. We are simultaneously launching another TÜBİTAK 1003 collaboration project with principal investigator Dr. Neşe Atabey from the Department of Medical Biology, School of Medicine at Dokuz Eylül University and in collaboration with Dr. Özden Yalçın Özuysal from the Department of Molecular Biology and Genetics at IYTE. Here, we will develop a new metastasis chip.

ACKNOWLEDGEMENT

I would like to thank the Turkish Patent Institute since they chose my patent to represent Turkey made it possible for me to participate in the Genevainvention exhibition.



**Contact Us to
Help Protect
Your Intellectual
Property too!**

FOR MORE INFORMATION

Dr. Devrim Pesen Okvur, İzmir Institute of Technology,

Web: <http://web.iyte.edu.tr/~devrimpesen/>

**WOULD YOU LIKE YOUR TECHNOLOGY PROJECT TO BE
HIGHLIGHTED IN THE NEXT ISSUE?**

Please send your article ideas to technosphere@atmosfertto.com for consideration.