PLASMA HEALTH CARE

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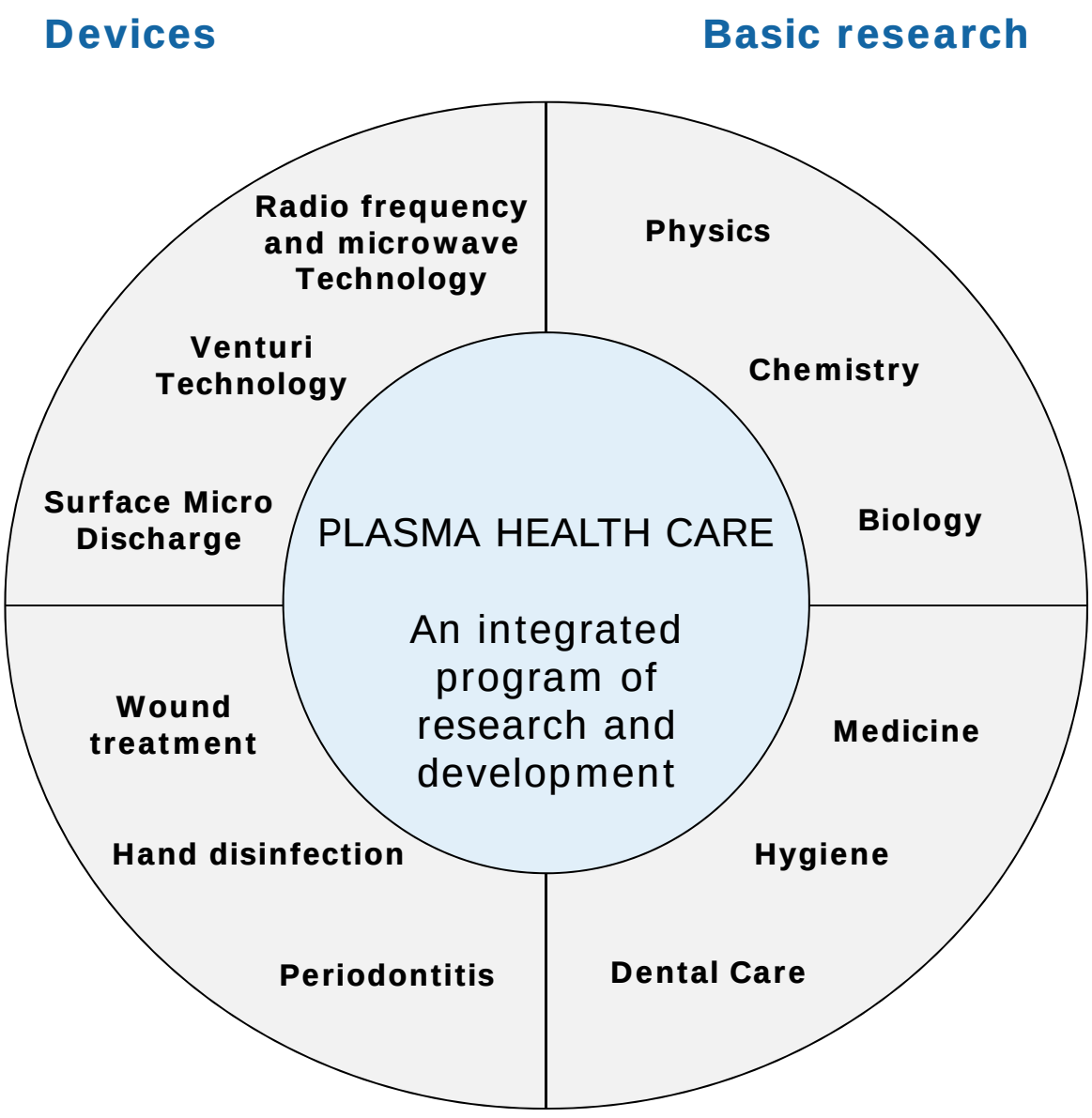
High-tech for your health



www.mpe.mpg.de/theory/plasma-med

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An integrated portfolio for product development

- **Robust platform technology for a wide range of applications**
- **Full compatibility with international safety regulations for reactive molecule production, UV emission and electrical requirements**
- **Cooperation network of biology, medicine and plasma chemistry institutes and specialists for basic and applied research**
- **Protected intellectual property of devices and methods**
- **Affordable technology solutions for an improved health care**
- **Offering a multitude of applications in medicine, hygiene, cosmetics and technology with a high market potential**

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An integrated program of research and development

From the laboratory to the hospital

Laboratory plasma devices were developed (with our industrial partner Adtec Plasma Technology Co. Ltd.) in accordance with the medical device directives for medical studies performed by our hospital partners. Current studies involve chronic wound treatment (phase I and II - disinfection; over 1600 treatments so far), wound healing and skin irritations (phase I and II – prurigo). Further studies are in preparation.

From the laboratory to industry

Laboratory prototypes are developed using different plasma production technologies. Major applications are in all areas of professional and personal hygiene, food hygiene and medicine. The aim is to cooperate with different (specialized) industry partners to develop these laboratory devices to industrial standards and to conduct all the tests (chemistry, biology, medicine, engineering) required for certification, within our network of cooperation partners.

From laboratory to people

A special development carried out in our laboratories concerns rechargeable hand-held OTC devices for domestic use at reasonable cost. There are many “personal” applications ranging from cosmetics to hygiene that can be addressed (from tooth brush disinfection to Deodorants and to athlete’s foot and tetanus prophylaxis. We are also looking into the possibilities for “plasma add-ons” for household appliances, where plasma disinfection may provide an added bonus.

A program for the benefit of

Patients

- Reduce the risk of hospital induced infections
- Provide contact-free and pain-free disinfection in seconds
- Alleviate pain caused by infections
- Alleviate skin irritations and reduce the risk of infection caused by scratching
- Promote faster healing
- Reduce hospitalization

Doctors

- Reduce skin irritations and allergic reactions in pre-surgical disinfection
- Decontaminate/disinfect equipment, fabrics and possibly whole rooms

Nursing staff

- Provide efficient disinfection in seconds
- Reduce the risk of skin irritations and allergic reactions
- Disinfection without waste products, chemicals etc., saving time, organization and storage space

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Basics

Plasma is a partly ionized gas and contains:

- **Neutral gas**
- **Charged particles**
- **Excited atoms / molecules**
- **Reactive species**
- **Light**
- **Electric field**
- **Heat**

1. **Plasma has bactericidal, fungicidal and virucidal properties.**
2. **Plasma ions can function as new medically active agents.**
3. **Depending on the desired application, plasmas can be designed individually by adding different gases, catalysts or known medically active agents.**
4. **Reactive species and active agents can be applied on a molecular level to the tissue - selectively and fast.**
5. **Excited atoms / molecules can increase the permeability of cell membranes and enhance penetration of active agents.**
6. **Plasma in appropriate dose and composition can stimulate and promote healing**

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Fields of application

Medicine – treating and healing diseases

- **Plasma Wound Care:** Treatment of chronic wounds
- **Plasma Dermatology**: Treatment of skin irritations and diseases
- **Plasma Dentistry**: Periodontitis prophylaxis
- **Plasma Surgery:** Infection control
- **Equipment Sterilization:** Efficient, mobile, portable

Hygiene – avoiding and containing diseases

Professional Hygiene:
- Prophylaxis against nosocomial and community associated infections in hospitals, medical practices, nursing homes and all public buildings (hand disinfection)
- Containment of diseases
- Food hygiene
- Water hygiene

Personal Hygiene:
- Treatment of athlete‘s foot
- Dental care and oral hygiene
- Home hygiene
- Reduction of perspiration-corrosive bacteria (plasma deodorant)

Cosmetics – improving appearance

Professional Cosmetics:
- Corrective surgery
- Scars cosmetics
- Dental cosmetics

Personal Cosmetics:
- Tooth bleaching
- Nail cosmetics
- Skin care

Technology – treating surfaces

- Surface modification
- Surface cleaning

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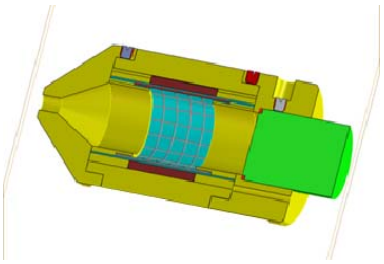
Basic research

Plasma Physics

Plasma design – mechanical devices, chemical composition, plasma production techniques, diagnostics of plasmas



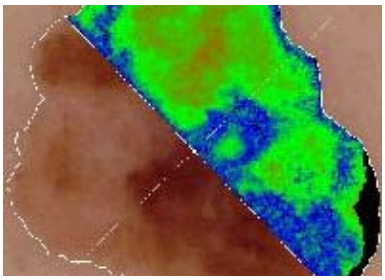
Plasma Technology

Development and optimization of plasma sources, miniaturization, up to the prototype level

(1) Nitrogen model
Ionization $e + N_2 \rightarrow N_2^+ + 2e$
Dissociation $e + N_2 \rightarrow 2N + e$
Dissociative recombination $e + N_2^+ \rightarrow N_2$
(2) Oxygen model
Ionization $e + O_2 \rightarrow O_2^+ + 2e$
Dissociation $e + O_2 \rightarrow 2O + e$
Dissociative attachment $e + O_2 \rightarrow O^- + O$
Recombination $O^- + O_2^+ \rightarrow O + O_2$
Dissociative recombination $O + O^- \rightarrow O_2 + e$

Plasma Chemistry

Simulation of the full chemical reaction network for different plasma sources



Data Analysis

Application oriented analysis of plasma – tissue effects, quantitative determination of plasma induced changes (e.g. wound healing)

Plasma Biology

Analysis of the plasma effects on eukaryotic, and prokaryotic cells, viruses, fungi and spores

Environmental effects, resistance tests, identification of basic biochemical processes

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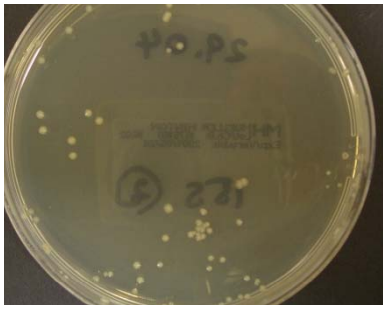
Applied research

Plasma Medicine

Currently: investigations of plasma wound treatment and prurigo skin diseases

Long term: plasma (design) pharmacology for different diseases



Plasma Microbiology

Quantitative in vitro and in vivo investigation of bactericidal, virucidal and fungicidal effects of plasmas

Plasma Hygiene

Nosocomial and CA infection control (including multi-resistant germs – e.g. MRSA), prevention and containment of contagious diseases, disinfection of medical devices, surface treatment (heat and UV sensitive surfaces)

Plasma Dental Care

Periodontitis prophylaxis, disinfection of dental cavities, general oral care, equipment disinfection

Plasma Food Hygiene

Disinfection of food containers, food surface disinfection, hygiene in food handling, preparation and packaging

(Photo: Smoked Fish at Zabars, New York)

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Different plasma production technologies

Plasma production by radio frequency or microwave-induced discharges:

These devices use a noble carrier gas (Ar, He, Ne), which can be supplemented with other gases to obtain different chemistry. Applications are seen in regenerative, prophylactic and therapeutic medicine. The estimated cost of these devices lies in the range of a few 10.000 €.

Venturi flow effect:

This is a plasma-jet device, that can operate in air or with appropriate “gas mixtures and additives” for plasma design. The special venturi flow effect allows atmospheric pressure plasma production in a local lower pressure environment. This makes plasma production easier and more efficient.
Applications are seen in dentistry, cosmetics and surgery.
The estimated cost of such a device lies below 10.000 €, depending on the configuration (including gas supply).

Surface Micro Discharge (SMD) Technology:

This is a platform technology where atmospheric plasmas can be produced over large areas with a power requirement of less than 0.5 W/cm^2. The electrode can be produced in any shape and is scalable to different sizes. The principle is a “surface micro discharge (SMD)”, where the plasma is generated via numerous microdischarges. Applications are seen in all areas of professional and personal hygiene, food hygiene and cosmetics. The estimated cost depends on the specific application. The SMD technology allows plasma sources for low budget applications.

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Plasma devices

Microwave plasma devices, which operate with noble gases:

MicroPlaSter β

This is a medical device used for the clinical trials – wound treatment and prurigo. It has a 6-electrode plasma torch at the end of a flexible arm. Two modes of operation exist - “plasma treatment” and “placebo treatment”. In the placebo mode only warm Argon gas comes out from the torch.

In cooperation with Adtec Plasma Technology Co. Ltd.

NanoPlaSter

This plasma torch contains one single electrode with an opening diameter of 2 mm. This torch is designed to treat small areas. In our research it is mainly used for biological experiments with cells and bacteria.

In cooperation with Adtec Plasma Technology Co. Ltd.

Plasma device, which uses the Venturi Effect:

VenturiPlaSter

This device has a Venturi nozzle on the inside. By applying pressures of a few bar of gas (ambient air, He, Ar, etc.) on one side, the pressure inside can be controlled between 180 and 1000 mbar. The plasma is produced in the low pressure region and is transported to the application site by the gas flow.

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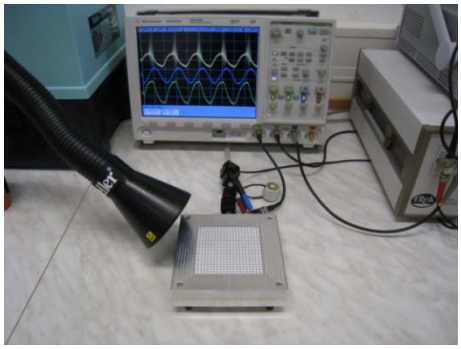
Plasma devices

Surface Micro Discharge (SMD) Technology operated with ambient air:

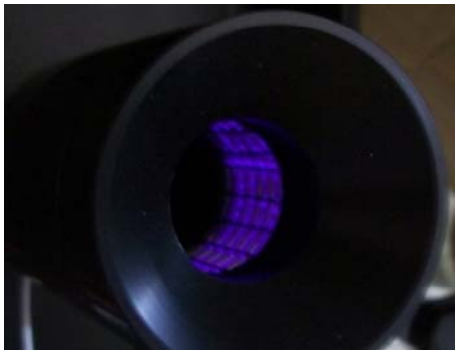
HandPlaSter

This device contains two SMD electrodes - one at the top and one at the bottom. Each electrode for example consists of a metal plate, an insulator plate and a mesh grid. The plasma is produced by applying AC voltage on the metal plate. The mesh grid is grounded.



FlatPlaSter

This device contains one SMD electrode.



CylindricalPlaSter

This device contains one cylindrical SMD electrode and a fan on the rear side in order to transport the plasma to the outside.

PersonalPlaSter

Small hand held device with a rechargeable battery. The plasma is produced by a cylindrical SMD electrode. A fan placed behind the electrode provides the plasma flow.

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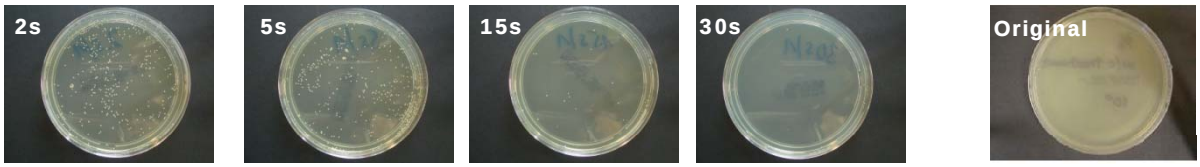
Examples of research results

1. Plasma has bactericidal effect

Different gram positive and gram negative bacteria were tested, including MRSA. Depending on the plasma device, a reduction in bacterial load (in vitro) by a factor of 100.000 or more was achieved in a few seconds to a few minutes. (Morfill et al., NJP 11, 115019, 2009)



Bactericidal effect of the Plasma produced by the HandPlaSter tested with Methicillin-Resistant *Staphylococcus Aureus* (MRSA). After a treatment time of approximately 10s a 100.000 bacterial reduction is achieved.

2. Bacterial resistance tests

Using a SMD electrode the bacterial resistance development of gram positive and gram negative bacteria was analyzed in detail. No primary or secondary resistance against the plasma treatment has been seen so far. (Zimmermann et al., in preparation, 2010)

3. Humidity tests

No significant performance changes were identified for SMD plasmas over a whole range of environmental parameters for gram positive and negative bacteria. (Shimizu et al., in preparation, 2010)

4. Plasma has fungicidal effect

Tests were made with Candida Albicans. Fungicidal efficiency was similar to bactericidal efficiency for all plasma productions. (Morfill et al., NJP 11, 115019, 2009)

5. Plasma has virucidal effect

Adenoviruses in liquid suspension were treated with plasma. Significant virucidal effects were observed after 4 min of plasma treatment using the SMD technology. (Zimmermann et al., in preparation, 2010)

6. Plasma reduction of spores

Bacillus atrophaeus spores were treated with DBD Plasmas at different humidity. Significant reduction of spores could be demonstrated in humid environments. (Hähnel et al., Plasma Processes and Polymers, 2010, 7, 244-249)

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Examples of research results

7. Effect of plasma on eukaryotic cells

Fibroblasts:

Bactericidal effect of plasma irradiated liquids increases for higher plasma dosages. However, at low dosages (where a bactericidal effect was already observed) plasma irradiated liquids have a stimulating effect on the proliferation of human skin fibroblasts. (Nosenko et al., NJP 11, 115013, 2009)

Blood cells:

No morphological effects were observed even after 10 minutes of plasma treatment. (Unpublished result, Pompl et al., 2007)

8. Mutagenicity tests

The mutagenicity of microwave plasma treatments was tested with the HPRT* assay in vitro with mammalian cells. No mutagenic effects were observed. (Karrer et al., in preparation, 2010)

(*hypoxanthinic-guanine phospho-ribosyl-transferase)

9. Clinical plasma trials on wound treatment

The aim of the study is to reduce the bacterial load in chronic leg wounds significantly, and to see if this alleviates pain and promotes healing. In a phase II study over 1600 treatments have been carried out so far. Significant bacterial load reduction could be demonstrated, as well as success in healing. No detrimental side effects were observed in this (worldwide) first plasma medicine study with humans. (Isbary et al., Brit. J. of Dermatology, accepted)




before after
with plasma treatment

before after
without plasma treatment

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Publications

- **Characterization of Microwave Plasma Torch for Decontamination**
  Tetsuji Shimizu, Bernd Steffes, René Pompl, Ferdinand Jamitzky, Wolfram Bunk, Katrin Ramrath, Matthias Georgi, Wilhelm Stolz, Hans-Ulrich Schmidt, Takuya Urayama, Shuitsu Fujii, Gregor Eugen Morfill
  Plasma Processes and Polymers 2008, 5, 577-582

- **Focus on Plasma Medicine**
  Gregor E. Morfill, Michael G. Kong and Julia L. Zimmermann
  New Journal of Physics 11 (2009) 115011 (8pp)

- **The effect of low-temperature plasma on bacteria as observed by repeated AFM imaging**
  René Pompl, Ferdinand Jamitzky, Tetsuji Shimizu, Bernd Steffes, Wolfram Bunk, Hans-Ulrich Schmidt, Matthias Georgi, Katrin Ramrath, Wilhelm Stolz, Robert W. Stark, Takuya Urayama, Shuitsu Fujii and Gregor E. Morfill
  New Journal of Physics 11 (2009) 115023 (11pp)

- **Nosocomial infections - a new approach towards preventive medicine using plasmas**
  Gregor E. Morfill, Tetsuji Shimizu, Bernd Steffes and Hans-Ulrich Schmidt
  New Journal of Physics 11 (2009) 115019 (10pp)

- **Designing plasmas for chronic wound disinfection**
  Tetyana Nosenko, Tetsuji Shimizu and Gregor E. Morfill
  New Journal of Physics 11 (2009) 115013 (19pp)

- **Plasma medicine: an introductory review**
  Michael G. Kong, Gerrit Kroesen, Gregor E. Morfill, Tetyana Nosenko, Tetsuji Shimizu, Jan van Dijk and Julia L. Zimmermann
  New Journal of Physics 11 (2009) 115012 (35pp)

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Publications

- **Characterization of Low-Temperature Microwave Plasma Treatment with and without UV Light for Disinfection**
  Tetsuji Shimizu, Tetyana Nosenko, Gregor E. Morfill, Takehiko Sato, Hans-Ulrich Schmidt and Takuya Urayama
  Plasma Processes and Polymers 2010, 7, 288-293

- **A first prospective randomized controlled trial to decrease bacterial load using cold atmospheric argon plasma on chronic wounds in patients**
  Georg Isbary, Gregor E. Morfill, Hans-Ulrich Schmidt, Matthias Georgi, Katrin Ramrath, Julia Heinlin, Sigrid Karrer, Michael Landthaler, Tetsuji Shimizu, Bernd Steffes, Wolfram Bunk, Roberto Monetti, Julia. L. Zimmermann, René Pompl and Wilhelm Stolz
  British Journal of Dermatology, accepted

- **Plasma applications in medicine with a special focus on dermatology**
  Julia Heinlin, Georg Isbary, Wilhelm Stolz, Gregor E. Morfill, Michael Landthaler, Tetsuji Shimizu, Bernd Steffes, Tetyana Nosenko, Julia L. Zimmermann and Sigrid Karrer
  Journal of the European Academy of Dermatology and Venereology, submitted

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Protected Intellectual Property

- **Method and means of spatial filtering**
  Determine the bacterial loads of wounds, validation of the sterilizing effects of the plasma treatments.
  (EU, US, JP Patents)

- **Plasma Torch**
  Plasma sources used for the treatment of living tissue for in-vivo applications in hospitals. Specifically for the treatment of larger chronic wounds such as ulcers.
  (EU, US, RU Patent Application)

- **Plasma Source**
  UV-free plasma source based on a Venturi or a Laval nozzle. Miniaturization.
  (EU, PCT Patent Application)

- **Non-thermal plasma for wound treatment and associated apparatus and method**
  Designer-plasma (as pharmaceutical) specifically designed for the treatment of biological tissue.
  (PCT Patent Application)

- **Applicator and corresponding method**
  Plasma applicator for VAC therapy on chronic wounds by Kinetic Concepts Inc.
  (PCT Patent Application)

- **Adaptive Mesh Electrode (Surface Micro Discharge Elctrode)**
  (PCT Patent Application)

- **Hand Plasma Dispenser (HandPlaSter)**
  (PCT Patent Application)

- **Penetrating Plasma**
  (PCT Patent Application)

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Cooperation

Germany:

- Max Planck Institute for Extraterrestrial Physics
- Max-Planck-Innovation GmbH
- Department of Dermatology, Hospital Schwabing, Munich
- Medizet Department Microbiology, Schwabing, Munich
- Department of Dermatology, University Hospital Regensburg
- Department of Neuropathology, TUM, Munich
- Institute of Experimental Oncology, TUM, Munich

Russia:

- Joint Institute for High Temperature, RAS
- Institute for Biomedical Problems, RAS
- Institute for Epidemiology and Microbiology, RAMS
- Institute for Theoretical and Experimental Biophysics, RAS
- Institute for Problems of Chemical Physics, RAS
- Institute for Physical Chemical Medicine, RAMS

USA:

- University of California, Berkeley

UK / Japan:

- Adtec Plasma Technology Co. Ltd.

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Further details about our cooperation partners and research can be found on our Webpage:
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