

Project Progress Summary

Section 1: PROJECT IDENTIFICATION Information to be provided for project identification		NOT CONFIDENTIAL
Title of the project		
TISSUE ENGINEERING OF LIVING BIOSENSORS TO EVALUATE RISKS FOR HEALTH BY PESTICIDES AFFECTING THE CHOLINERGIC NEUROTRANSMITTER SYSTEM		
Acronym of the project		
SENS-PESTI		
Type of contract RTD		Total project cost (in euro) EUR 1,607,136 (one million six hundred and seven thousand one hundred and thirty-six €)
Contract number QLK4-CT-2002-02264	Duration (in months) 36 Months	EU contribution (in euro) EUR 1,404,153 (one million four hundred and four thousand one hundred and fifty-three €)
Commencement date 1 January 2003		Period covered by the progress report (e.g. 1 February 2000 – 31 January 2001) 1 January-31 December 2003
PROJECT COORDINATOR <u>carla falugi</u>		
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Key words (5 maximum - Please include specific keywords that best describe the project.). Neurotoxic pesticides, cholinergic system; differentiation; embryonic malformation; disease; biosensor		
World wide web address (the project's www address) www.biologia.unige.it/falugi/senspesti.html		

List of participants Provide all partners' details including their legal status in the contract i.e., contractor, assistant contractor (to which contractor?).

◆ **Partner N°2: contractor**

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Subcontractors:

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Section 2: Project Progress Report

NOT CONFIDENTIAL

(2 pages maximum.. Use short sentences. Be factual. Avoid technical terms as much as possible)

Objectives of the first 12 months of work:

- 1- To identify the mainly used neurotoxic pesticides, presenting characteristics that make them suitable to be used as a general model of their action.**
- 2- To identify the mechanism of action of the neurotoxic pesticides, in selected biological models. The models should be very simple, and bioethically compatible.**
- 3- To expose the selected models to the pesticides at concentrations under the commonly considered no-effect concentration (NOEC) and admissible daily intake (ADI) for man, in order to understand the chronic effects, and in the future work to identify “ safe” pesticides and concentrations.**
- 4- To establish parameters that allow to correlate the effects on the biological models to human embryonic differentiation, by use of mammalian and human cell cultures committed to differentiation.**
- 5- To preliminarily investigate the chemico-physical effects of the pesticides, that may be used as markers of risk to human health.**
- 6- To supply the information to the industrial partner, to be used for the building of a biosensor, based on these parameters.**
- 7- To establish the physiological functions of molecules belonging to the neurotransmitter system which are targets of the pesticides action, in developing embryos, differentiating cell cultures and in disease.**

During the first year of project, all the expected deliverables were achieved by the partners.

Results and Milestones®

- 1- After a survey of several pesticides, during the first kick-off meeting we have chosen 6 pesticides, e.g. among organophosphates: *diazinon*, *phenthoate*, *chlorpyrifos* and *malathion*, among carbamates: *carbaryl* and *carbofuran*, which all are in use in greenhouses and in the fields. The use in greenhouses is more dangerous for man. In order to confirm the choice, we tested several organophosphate and carbamate insecticides, both the formulated commercial mixtures and the active principles. The effects of the commercial products were to be referred to the concentration of the active principles in the mixtures. For instance, the formulated commercial compound Basudin contains 20% diazinon (see the report 1, not confidential). Moreover, according to what we decided during the kick-off meeting, the chemical and physical properties (solubility, pH, persistence, hydrophobicity, optimal temperature, time of degradation, etc.) of each pesticide was found by use of an official data base, and the target molecules were identified by our experiments, together with reports available in the literature.

We established the protocol of dilution of the pesticides (see the protocols 1, 1a and 1b of University of Szeged), the IC50 concentrations of pesticides (report 2, USZEGED), and the concentrations corresponding to the currently used ADI for man for each pesticide (reported in the available data bases).

- 2- The selected biological models were at different organisation levels: cultured cells, spheroids of cultured cells and developing early embryos of invertebrates and vertebrates, at stages prior to the onset of sensorial activity. We added other models to the ones reported in the technical annex: a) insect heads, to verify the sensitivity of the insects (target of the pesticides; b): to the adult bone marrow stem cells we added NT2 cells (teratocarcinoma, committed to neural differentiation) to speed up the finding of the effects of pesticides on differentiating nervous cells.
- 3- After several experiments, we decided to follow, besides the effects on AChE activity, also the **direct effects on muscarinic receptors**, because these last effects are exerted on the electrical behaviour of the cells and embryos, useful for establishing parameters of sensitivity in the **biosensor**, which is the main objective of the project.

Actually, we found that the electrical effects modulated by muscarinic receptors on K⁺ electrical channels are about 100-fold more sensitive than morphological and biochemical effects, as they are still present at concentrations around the ADI for man. Thus, when no response is found with the electrophysiological recordings we can consider that the investigated single dose of pesticide is "safe" for man (report 3, confidential). On the contrary, the membrane depolarisation linked to modulation of Ca²⁺ is affected, but not very sensitive.

On the other hand, we found, during our previous investigation that low doses not affecting embryonic development and viability of the zebra fish embryos, become dangerous when repeated. Thus, for the next year we will investigate the effects of the apparently safe doses, repeated during development and differentiation (chronic exposure to low doses), also with electrophysiological experiments.

Previous results were also obtained by exposing embryos to low doses (no-effect) of pesticides together with low doses of metals (such as mercury). The results seem to be interesting, although up to date these experiments were only performed on the sea urchin early embryo model (Thesis, UGE).

Another important outcome for the moment is the finding that, while several international Environmental Protection Agencies (Canada, USA) use a validated protocol of spermotoxicity to evaluate the environmental quality, we realised that this test protocol is useful for metals, IPA and so on, but is scarcely sensitive for neurotoxic pesticides, because after 1 h exposure to neurotoxic pesticides (as it is reported in the validated protocols) sperms do not lose the fertilising ability, unless the pesticides are very concentrated. This analysis acquires value only if it is followed by embryo toxicity examinations e.g. nuclear status analysis, etc: see the attached report labelled as "acetylcholine").

Benefits and Beneficiaries:

Improvement of the standard validated tests for risk assessment, (beneficiaries: policy makers, national and regional EPAs)

Assessment of security in the use of active principles (beneficiaries: policy makers, pharmaceutical Industry)

Assessment of the doses of active principles that are really “safe” for man and effective for pest control (beneficiaries: pharmaceutical industry, consumers)

Deliverables achieved during the first year:				
Deliverable No ¹	Deliverable title	Deliver date ²	Nature	Dissemination level ⁴
D a	Project website	M2	D	RE
D b	Glossy project brochure	M4	O	PU
D1.1	<u>Exchange of models, including technical support:</u> <i>Personnel from UGE, and from IBMT had a 2 months stages in the Laboratory of YORK, in order to learn adult stem cells culture and differentiation methods</i>	M6	O	CO
D1.2	<u>Standardised protocol of all procedures</u> <i>USZE supplied 1- protocols for solutions and doses of the hydrophobic compound; 2- databases of EC50 for each selected pesticide (and commercial formulates) in different cells, tissues and organisms, including man</i>	M12	Me	RE
D3.1	<u>Protocols for differentiation from adult bone marrow-derived stem cells</u> <i>These protocols were supplied by YORK to all the Partners</i>	M12	Da	CO
D3.4	<u>Annual report to the Commission</u> <i>see report 1 (UGE)report 2 and report 3 (TUD</i>	M12	R	RE
D4.1	<u>Design and fabrication of suitable 3D microcapillary systems</u> <i>This task was performed by IBMT, in cooperation with the technical SME THINXX</i>	M4	D	CO
D4.2	<u>Retinospheroid cultures according to different developmental stages for implication on microcapillary arrays</u> <i>This task was performed by TUD, who also used the 3-D nervous cells cultures for the first exposure experiments. The 3-D cultures contain the different cell types belonging to the functional nervous tissue</i>	M5	O	CO
D4.3	<u>Report of molecular and enzyme activity data for correlation with sensor system output</u> <i>All the biological partners delivered the results to IBMT. A visit was exchanged between IBMT, UGE, USZE and the subcontractor 1 (who was beginning the electrophysiological recordings after exposure of nervous cells)</i>	M9	R	CO

¹ Deliverable numbers in order of delivery dates: D1 – Dn

SECOND PERIOD (2004)

During the first two years of work, almost all the previewed deliverables were completed, as well as WP 4, completed in the forecasted period. The results gave us the possibility to reach the objective previewed in the 3rd year.

By the scientific point of view:

Partner 4 found the concentrations of the active principles that are optimal for insects, and we realised that these concentrations are from 100 to 1000 fold **lesser** than the corresponding ones suggested on the labels of the products for agricultural and gardening purposes.

- I- The YORK group (Partner 2) found that these concentrations (the Zoltan's ones) are able to affect **human** bone marrow cells **differentiation**, including the synthesis of particular molecules
- II- The TUD group (Partner 3) found that the same concentrations may affect **development** of fish embryos, and adult blood BuChE activity, including some side effects (aryl-acyl-amidases). He found the effects of toxication in retinospheroids and carried out the first measurements with the biosensor of Hagen Thielecke (Partner 5)
- III- IBMT (Partner 5) has obtained either the conceptual design and the crafted biosensor, ready to be experimented with our models, and obtained the first results with retinospheroids were obtained
- IV- UGE (Partner 1) found that different organisms are affected in **different** ways by the active principles: e.g. chick embryos and (more) mammalian cells are very sensitive, while other models are less sensitive, both to impairing of acetylcholinesterase activity and embryonic differentiation. We feel that this is because slightly impairing acetylcholinesterase enhances the activity of acetylcholine at receptorial sites, causing a hormetic response. This work gave us the opportunity to identify the relevant role of acetylcholine during early differentiation, at least in two models. This is also confirmed by other researchers, that found a toxic activity of acetylcholinesterase on cultured neural cells.
- V- Control and exposed tissues and homogenates were sent to USZE, who performed spectrophotometric and radiometric assays, showing the effects of exposures on the enzymes associated to the cholinergic system

² Month in which the deliverables will be available. Month 0 marking the start of the project, and all delivery dates being relative to this start date.

³ Please indicate the nature of the deliverable using one of the following codes:

R = Report
P = Prototype
D = Demonstrator
O = Other

⁴ Please indicate the dissemination level using one of the following codes:

PU = Public
RE = Restricted to a group specified by the consortium (including the Commission Services).
CO = Confidential, only for members of the consortium (including the Commission Services).

D1.3	<p>Report on biomarkers related to WP1</p> <p>Endpoints: Following application of pesticides (task 1, 2), changes in the following molecular markers will be established: ChE activities (USZE and TUD) in progress, their molecular forms, glycosylation, protein complex formation, and their novel side activity aryl acylamidase (AAA) TUD, nicotinic (two papers submitted Trombino) and muscarinic AChRs (see paper JCB), (UGE) ChAT (USZE), cytochrome oxidase, glutamate, GABA, Wnt, and Notch by standard enzyme and protein biochemistry, blotting and PCR technologies</p> <p>Biomarkers: As cellular and tissue biomarkers cell proliferation (report UGE), apoptosis, retinal cell differentiation (photoreceptors, ganglion and amacrine, Müller cells), axon growth (of cerebellar granules), retinal lamina and network formation (synaptic plexiform layers in spheroids) by immunocytochemistry, electron and confocal microscopy, in situ hybridisation (Report TUD), and molecular cloning (PCR). The in vitro data as obtained were compared with similar data from the chick and mouse embryo, and also with those from the sea urchin and human stem cells (see WP3).</p>	M15	R	RE
D1.4	<p>Publication of results</p> <p>The first papers related to WP1 were submitted to peer review journals and prepared for report to the E C</p>	M15	R	PU
D2.1	<p>List of effects of exposures to pesticides in embryos and cell/tissue cultures (WP2).</p> <p>onset of cholinesterase expression (AChE and BChE), (TUD, USZE). Individuation of a side activity found on all cholinesterase (ChE) and aryl acylamidase (AAA) activity as a possible target for pesticides, (TUD*) in control and exposed developing organs and in 3-D neural cultures (TUD, IBMT).</p> <p>Characterisation of cell morphology and cytoskeletons supporting neural morphology (neurotubulins, neurofilaments). Immunocytochemistry, electron microscopy. Extracellular matrix release and function. Comparison with stem cells. Analysis of the onset of expression and distribution of acetylcholine receptors (muscarinic and nicotinic, and their different molecular forms) by immunocytochemistry electron and confocal microscopy, and molecular cloning (polymerase chain reaction, PCR), (UGE).</p> <p>Intracellular ion dynamics (Ca⁺⁺ and K⁺) related to ACh receptors excitation/blockade in control and exposed samples (subcontractor 1)</p> <p>Comparison among the different anti-cholinesterase pesticides, comparison with an anti-fouling anti-cholinesterase of natural origin at low doses.</p>	M15	Da	CO
D2.2	<p>Publication of results</p> <p>Effects on sea urchin fertilization and early development submitted to European J. of Histochemistry</p> <p>3 partners presented posters and communications at the INTERNATIONAL Cholinesterase MEETING held in Perugia (Italy) September 26-30 2004</p>	M15	R	PU
D2.3	<p>Annual and final reports</p> <p>Besides the reports, all the results of the first 18 months were presented at the midterm meeting</p>	M 24	R	RE
D3.2	<p>Distribution of cells and cell homogenates to other laboratories</p> <p>Cells were sent from York, UGE and TUD to USZE, for further analyses</p>	M12 -30	Me	CO
D3.3	<p>Report on the effect of pesticides on stem cell differentiation</p> <p>Report was distributed to the Partner laboratories and presented at the midterm meeting</p>	M30	R	CO

THIRD REPORTING PERIOD (2005):

During the third year of work, the last deliverables were achieved, and the biosensor based on planar adult human stem cells was designed and performed. Its functionality was demonstrated at the final meeting and workshop, held in Parma, the 23-34 october, 2005. According to the differentiation of the cells inserted, the biosensor may mimick the responses of the embryonic parts and tissues to stress from food or environment.

The biosensor is ductile and may be subject to amplification and further uses, for both environmental diagnosis, analyses of food, and may adapt its function for other dangers present in the environment, of industrial or natural origin

Benefits and Beneficiaries

All the partners enhanced their productivity, and formed Ph. D. students specialised in the field of cytotoxicology. Up to date, 12 papers were produced, and others are ready to be published.

By domestic conferences, public was informed about the possible choice for quality of life

Governmental agencies of the involved Partners showed interest for our work.

DL.	Deliverables list				
Deliverable No ⁵	Deliverable title	Delivery date ⁶	Nature ⁷	Dissemination level ⁸	
D3.2	<u>Distribution of cells and cell homogenates to other laboratories</u> <i>This task was continuously performed, mainly towards USZE, who analysed the enzyme activity of all the samples delivered by the other samples</i>	M12-30	Me	CO	
D3.3	<u>Report on the effect of pesticides on stem cell differentiation</u> <i>Mesenchymal Stem cells and Umbilical Chord cells were used for studying the effects of exposures on human tissue differentiation. The effects were studied towards differentiation to a number of phenotypes, and the most affected phenotypes were osteogenesis and haemopoiesis. Two papers were submitted to peer reviewed journals.</i>	M30	R	CO	
D5.5	<u>Documentation about correlation of sensor system output and cholinesterase data</u> <i>This was performed in cooperation between USZE, TUD and IBMT. Papers were prepared and submitted to the EC (3d periodic report)</i>	M20	R	CO	
D6.1	<u>Report about impedance measurement of human adult stem cells and correlation with cholinesterase data</u> <i>Presented in the 3rd periodic report. Two biosensors prototypes were presented at the last meeting and workshop (23-24 october 2005, Parma, Italy) see www.SENS-PESTI.com</i>	M34	R	CO	
D d	<u>Final complete report to the Commission</u>				

⁵ Deliverable numbers in order of delivery dates: D1 – Dn

Dissemination and Exploitation

- ✓ A Consortium agreement with exploitation plan was drawn up before the start of the project and sent to the Commission for information.
- ✓ The partners mainly involved in exploitation were P5 (IBMT) and the subcontractor (ThinXXS). Their work is aimed to this result, and the man/months for this objective was 15 of the total 36
- ✓ Partner 5 (IBMT, whose scientific representing person is Hagen Thielecke) has already realized a workshop and invited the food industry of her regional area (Saarland, Rheinland-Pfalz, Baden-Württemberg) in Germany near to France and Luxembourg, to prepare an industrial network of these industrial partners. They are interested to evaluate a functional screening system (e.g. Döhler Euro-Citrus Natural Beverage Ingredients GmbH, Darmstadt, Germany; Dr. Markus Wydra - with letter of intent for collaboration)
- ✓ These industrial partners will be invited in the workshops located in Germany for evaluation and testing of our prototype: (German & French Food Industry -coordinated by IBMT)
- ✓ The objective of the exploitation will be the biosensor (product, and know how to extend the use of the biosensor to other items). Moreover, a series of conversion parameters will be identified for the use of other cells, to extend the possible exploitation to other areas.

- **Steps envisaged towards full exploitation:** the above described steps will also bring advantage to the small companies involved as a subcontractor in the production and use of it. The aim of the Company is to prepare the biosensor with selected materials and to distribute it to other Companies for a wider commercialisation and use of it.
- **Perceived obstacles for exploitation:** at present, the culture of human stem cells is very expensive, as this kind of work is relatively recent. Our aim was to make this work routinary and thus to lower the costs of the final product
- Is it envisaged that the project will result in publications in scientific journals, books, reports, participation at conferences with published proceedings. This will not be completely obtained within 3 years, because of the length of journals referee, proof correction, printing processes. The publications will regard the scientific part of the work (relative to WP1, WP2, WP3).
Actually, some papers are still in press, or waiting for peer review

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- The presence at the meetings of the Advisory Committee (including Industry, Policy makers, Consumers and Environmental Protection Agencies) constitutes a guarantee for all these social bodies. In this way, a dialogue is opened so that the potentiality of the industries will be
- Promote biotechnical development and new professional figures for environmental control.
- ✓ To reassure the consumers of agricultural products about their harmlessness.

THE BIOSENSOR Exploitation Plan:

In this project, commercial exploitations as well as profit could be expected in nearest future. With reference to the services and knowledge of the other partners, the main results are related to the possibility of construction and rearranging the information flow as well as technology (cell and tissue-based bio-electronic microstructures) between customers and services (in direct collaboration with an industrial subcontractor). Clients can get access to existing services and should gain guidance for the product developments according to their own demands, available prototypes, fabrications and final certification.

Microsystems and special bio-hybrid systems have potentially wide industrial applications and the markets are estimated to be large. Academic research groups as well as industry (especially in biohybrid systems / cell and tissue based micro-systems, biomedical engineering, medicine and informatics communities) are potentially interested in the services of the cluster and it may be expected, that many end-users will be targeted throughout the project.

The development of the biotechnological total market increased from the year 1997 until 2000 from 2529.9 billion Euros to 2835.4 billion Euros according to the demands of the health, food and environmental sections of approximately 11%, a further increase will be expected until the year 2005 up to 3432.1 billion Euros (up to further ~ 17%). The European area including East Europe will also expand the biotechnological market and development concerning novel drugs, therapies and diagnosis in the health section, high throughput screening modules, fast, specific, reproducible online monitoring systems for analytical screenings of drugs, medical products as well as for environmental pollution, toxic agents, pesticides, war fares and food compounds. Therefore, the three important market sections health, food, environment will define the biotechnology and their products worldwide, and will create also common developmental R&D areas as well as common profits by overlapping devices, screening modules and test systems.

Action fields:

- ✓ Publishing of a web page for the marketing of services and bio-hybrid systems for pesticide analytics.
- ✓ Preparation of a cluster presentation in collaboration with consortium partners.
- ✓ Preparation of a marketing pack of brochures and publicity material.
- ✓ Organisation of seminars, workshops and open days on bio-hybrid technology and bioanalysis.

- ✓ Conducting feasibility studies and trial analyses for potential customers.
- ✓ Preparation of case studies to show the consortium's expertise in the testing and analysis of pesticides using the developed bio-hybrid systems.

- ✓ Publications on related activities in international journals and periodicals.
- ✓ Attendance at suitable trade shows and exhibitions.
- ✓ Participation in scientific conferences & workshops
- ✓ Participation in appropriate cluster workshops.
- ✓ Interactions with other ongoing or proposed research activities at European or other international levels will be pursued. This will include communication with user clubs available through networks.
- ✓ Some examples were chosen for application areas in the field of environment, pharmaceutical market, employment, food industry and agriculture. The device is of great utility not only for insecticides, but also for any environmental, food, work situation impinging on the nervous system functionality.
- ✓ The network of the consortium will support local and European companies, specifically pharmaceutical, food, environmental and microsystem industry. As a service and bio-hybrid systems provider the partners will offer to customers information about bioelectronic microsystems, feasibility studies, and analytical tests with specified cell and tissue models and bioelectronic microstructures for functional screening.

Applied R&D activities:

- ✓ Public Relations material (brochures, posters, presentations and displays, newsletter)
- ✓ Workshops and internal training
- ✓ Company support by means of e.g. feasibility studies
- ✓ Presentation of a prototype
- Distribution of the biosensor(s) to Laboratories of Environmental Protection Agencies
- ✓ Distribution of Scientific information about the interference of neurotoxic molecules and human developmental events to scientific users and medical classes

DISSEMINATION OF RESULTS

The co-ordinator shall provide, by contract signature, a publishable summary of the project, which can be easily disseminated and distributed to the public. In addition, not later than the first report, the co-ordinator shall provide to the Commission, a publication (leaflet or brochure), summarising the main objectives of the project. This publication shall be formulated in layman's language in order to be easily readable by non-specialists.

The dissemination outside the project community will be gauged through the interest and feedback from end-users: The results will be available in a variety of ways

- ✓ For the European Community; reports during the procedure and final reports;
- ✓ For Scientific Users, through Publication in International Journals and presentation in Specific Meetings and Congresses;

- ✓ Regularly updated website
- ✓ Papers
- ✓ Materials available to other partners
- ✓ Symposiums
- ✓ Results transferred to the EC
- ✓ Scientific Community and others
- ✓ Biotechnology Companies
- ✓ Managers
- ✓ The lay public
- ✓ Policy makers.

All the dissemination material will be communicated to the Commission.

Dissemination of risk for health assessment

✓ Risk assessment will be stated during the WP 1,2,3 experiments, because the anomalies found in morphological, metabolic, cytological and genetic features will be correlated with epidemiological studies.

✓ Dissemination of these results will be performed by publications in Scientific journals and booklets to be sent to the EU Commission, Ministry of Health, Ministry of Environment, and other, as suggested by the European Commission, and to Policy makers of each Partner Country

✓ For the General Public, an accurate policy will be decided together, because the public information media tend to ingenerate alarm in citizens. The most important knowledge for the public is how to avoid risks, and this may be achieved by information through dedicated channels (web sites, public conferences, etc).

✓ = not yet achieved

✓ = already performed

Publications:

1-Boopathy and Layer (2004): *The protein Journal*, Vol 23 (5), pp 325 -333

2-Bytyqi et al. (2004). *European Journal of Neuroscience* 20, 2953-2962

3-Etheridge et al. (2004). *Stem Cells* 22, 849-860

2-Trombino et al. (2004): *Cancer research* 64, pp 135-145

3-Angelini et al. (2004) *European Journal of Histochemistry*, 36, pp 120-131

4-Trombino et al. (2004) *Current Medical Chemistry. - Anti-cancer agents* 4 in press

5-Angelini.....Thielecke et al (2004): in *Echinodermata* (V. Matranga ed.), Vol 2 of *Marine Molecular Biotechnology*, Series editor: W.E.G. Müller; Springer-Verlag GmbH, Auslieferungs-Gesellschaft, Heidelberg.

6-Aluigi et al. (2005) *Chemical-biological interactions*

7-Aluigi et al., (2006) *CREDO Newsletters* (issue of june, 2006)

moreover, other papers are still in preparation, or submitted:

- a) (UGE) Trombino S, Bisio A, Aluigi MG, Angelini C., Gallus L., Rakonczay Z(*), and Falugi C. (submitted) Effects of Organophosphate Compounds on Nt2 Cells Proliferation are Exerted through Multiple Mechanisms;
- b) (YORK) Martin J. Hoogduijn, Paul G. Genever (submitted)The regulation of Mesenchymal Stem Cells by Nicotinic and Muscarinic Receptors and the interference by chlorpyrifos-oxon.
- c) (YORK) M.J. Hoogduijn^{*†}, Rakonczay⁺, P.G. Genever (Submitted)The effects of Pesticides targeting the Cholinergic system on human Mesenchymal Stem Cells
- d) (YORK) I.S. Hitchcock,* M.J. Hoogduijn, G.J. Spencer, P.G. Genever (submitted) Effects of Organophosphate and Carbamate Pesticides on Adult Human Hematopoietic Progenitor Cells

IBMT is preparing publications and advertisement materials about the biosensors.