THE UNIVERSITY OF WESTERN ONTARIO
BIOHAZARDOUS AGENTS REGISTRY FORM
Approved Biohazards Subcommittee: September 25, 2009
Biosafety Website: www.uwo.ca/humanresources/biosafety/

This form must be completed by each Principal Investigator holding a grant administered by the University of Western Ontario or in charge of a laboratory/facility where the use of Level 1, 2 or 3 biohazardous agents is described in the laboratory or animal work proposed. The form must also be completed if any work is proposed involving animals carrying zoonotic agents infectious to humans or involving plants, fungi, or insects that require Public Health Agency of Canada (PHAC) or Canadian Food Inspection Agency (CFIA) permits.

This form must be updated at least every 3 years or when there are changes to the biohazards being used.

Containment Levels will be established in accordance with Laboratory Biosafety Guidelines, 3rd edition, 2004, Public Health Agency of Canada (PHAC) or Containment Standards for Veterinary Facilities, 1st edition 1996, Canadian Food Inspection Agency (CFIA).

Completed forms are to be returned to Occupational Health and Safety, (OHS), (Support Services Building, Room 4190) for distribution to the Biohazard Subcommittee. For questions regarding this form, please contact the Biosafety Officer at extension 81135 or biosafety@uwo.ca. If there are changes to the information on this form (excluding grant title and funding agencies), contact Occupational Health and Safety for a modification form. See website: www.uwo.ca/humanresources/biosafety

PRINCIPAL INVESTIGATOR	Dr. Jim Xu XUAN
SIGNATURE	
DEPARTMENT	Surgery
ADDRESS	Rm 2-F-222 375 South St (London)
PHONE NUMBER	661 2111 ext 23412
EMERGENCY PHONE NUMBER(S)	519 667 6552
EMAIL	jxuan@uwo.ca

Location of experimental work to be carried out: Building(s) HSB Room(s) Rm 222

*For work being performed at Institutions affiliated with the University of Western Ontario, the Safety Officer for the Institution where experiments will take place must sign the form prior to its being sent to the University of Western Ontario Biosafety Officer (See Section 12.0, Approvals).

FUNDING AGENCY/AGENCIES: OICR
GRANT TITLE(S): Molecular diagnosis and Therapy of prostate cancer by UTMD technology in combination with Engineered mouse models

PLEASE ATTACH A BRIEF DESCRIPTION OF YOUR WORK THAT EXPLAINS THE BIOHAZARDS USED AND HOW THEY WILL BE USED. PROJECTS SUBMITTED WITHOUT A SUMMARY WILL NOT BE REVIEWED. A GRANT SUMMARY PAGE MAYBE ADEQUATE IF IT PROVIDES SUFFICIENT DETAIL ABOUT EACH BIOHAZARD USED.

Names of all personnel working under Principal Investigators supervision in this location:

Vida Khatamianfar
Haixing Xuan
Tao Cheng

*** DESCRIPTION MUST BE ATTACHED TO THIS FORM OR PROJECT WILL NOT BE REVIEWED***

1.0 Microorganisms

1.1 Does your work involve the use of biological agents? ☒ YES ○ NO
(including but not limited to bacteria and other microorganisms, viruses, prions, parasites or pathogens of plant or animal origin)? If no, please proceed to Section 2.0

Do you use microorganisms that require a permit from the CFIA? ☒ YES ○ NO
If YES, please give the name of the species. E. coli DH5α
What is the origin of the microorganism(s)?
Please describe the risk (if any) of escape and how this will be mitigated:
Autoclaved.

Please attach the CFIA permit.
Please describe any CFIA permit conditions:

1.2 Please complete the table below:

Name of Biological agent(s)*	Is it known to be a human pathogen? YES/NO	Is it known to be an animal pathogen? YES/NO	Is it known to be a zoonotic agent? YES/NO	Maximum quantity to be cultured at one time? (in Litres)	Source/ Supplier	PHAC or CFIA Containment Level
E. coli DH5α.	○ Yes ☒ No	○ Yes ☒ No	○ Yes ☒ No	1 liter		○ 1 ☒ 2 ○ 3
	○ Yes ○ No	○ Yes ○ No	○ Yes ○ No			○ 1 ○ 2 ○ 3
	○ Yes ○ No	○ Yes ○ No	○ Yes ○ No			○ 1 ○ 2 ○ 3
	○ Yes ○ No	○ Yes ○ No	○ Yes ○ No			○ 1 ○ 2 ○ 3

*Please attach a Material Safety Data Sheet or equivalent from the supplier.

2.0 Cell Culture

2.1 Does your work involve the use of cell cultures? ☒ YES ○ NO
If no, please proceed to Section 3.0

2.2 Please indicate the type of primary cells (i.e. derived from fresh tissue) that will be grown in culture:

Cell Type	Is this cell type used in your work?	Source of Primary Cell Culture Tissue	AUS Protocol Number
Human	☒ Yes ○ No	PC3	Not applicable
Rodent	☒ Yes ○ No	NIH 3T3	
Non-human primate	○ Yes ○ No		
Other (specify)	○ Yes ○ No		

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2.3 Please indicate the type of established cells that will be grown in culture in:

Cell Type	Is this cell type used in your work?	Specific cell line(s)*	Supplier / Source
Human	⊗Yes O No	PC3	ATCC
Rodent	⊗Yes O No	NIH 3T3	ATCC
Non-human primate	O Yes ⊗No		
Other (specify)	O Yes ⊗No		

*Please attach a Material Safety Data Sheet or equivalent from the supplier. (For more information, see www.atcc.org) all are available from ATCC.

2.4 For above named cell types(s) indicate PHAC or CFIA containment level required O 1 ⊗2 O 3

3.0 Use of Human Source Materials

3.1 Does your work involve the use of human source materials? O YES ⊗NO
If no, please proceed to Section 4.0

3.2 Indicate in the table below the Human Source Material to be used.

Human Source Material	**Source/Supplier /Company Name**	**Is Human Source Material Infected With An Infectious Agent? YES/NO**	**Name of Infectious Agent (If applicable)**	**PHAC or CFIA Containment Level (Select one)**
Human Blood (whole) or other Body Fluid		O Yes ⊗No O Unknown		O 1 O 2 O 3
Human Blood (fraction) or other Body Fluid		O Yes ⊗No O Unknown		O 1 O 2 O 3
Human Organs or Tissues (unpreserved)		O Yes ⊗No O Unknown		O 1 O 2 O 3
Human Organs or Tissues (preserved)		Not Applicable		Not Applicable

4.0 Genetically Modified Organisms and Cell lines

4.1 Will genetic modifications be made to the microorganisms, biological agents, or cells described in Sections 1.0 and 2.0? ⊗YES O NO If no, please proceed to Section 5.0

4.2 Will genetic modification(s) involving plasmids be done? O YES, complete table below ⊗NO

Bacteria Used for Cloning *	Plasmid(s) *	Source of Plasmid	Gene Transfected	Describe the change that results
SV40TAg.	Only T antigen gene used.			

* Please attach a Material Data Sheet or equivalent if available.

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4.3 Will genetic modification(s) involving viral vectors be made? O YES, complete table below ~~O~~ NO

Virus Used for Vector Construction	Vector(s) *	Source of Vector	Gene(s) Transduced	Describe the change that results

* Please attach a Material Safety Data Sheet or equivalent.

4.4 Will genetic sequences from the following be involved?

- HIV O YES, please specify _____ ~~O~~ NO
- HTLV 1 or 2 or genes from any Level 1 or Level 2 pathogens O YES, specify _____ ~~O~~ NO
- SV 40 Large T antigen ~~O~~ YES O NO
- E1A oncogene O YES ~~O~~ NO
- Known oncogenes O YES, please specify _____ ~~O~~ NO
- Other human or animal pathogen and or their toxins O YES, please specify _____ ~~O~~ NO

4.5 Will virus be replication defective? O YES ~~O~~ NO

4.6 Will virus be infectious to humans or animals? O YES ~~O~~ NO

4.7 Will this be expected to increase the containment level required? O YES ~~O~~ NO

5.0 Human Gene Therapy Trials

5.1 Will human clinical trials be conducted involving a biological agent? O YES ~~O~~ NO
(including but not limited to microorganisms, viruses, prions, parasites or pathogens of plant or animal origin)
If no, please proceed to Section 6.0

5.2 If YES, please specify which biological agent will be used: _____
Please attach a full description of the biological agent.

5.2 Will the biological agent be able to replicate in the host? O YES O NO

5.3 How will the biological agent be administered? _____

5.4 Please give the Health Care Facility where the clinical trial will be conducted:_____

5.5 Has human ethics approval been obtained? O YES, number: _____ O NO O PENDING

6.0 Animal Experiments

6.1 Will live animals be used? ~~O~~ YES O NO If no, please proceed to section 7.0

6.2 Name of animal species to be used 2008-98 mouse C57BL6 129

6.3 AUS protocol # 2008-098

6.4 Will any of the agents listed in section 4.0 be used in live animals O YES, specify: _____ ~~O~~ NO

6.5 Will the agent(s) be shed by the animal: O YES ~~O~~ NO, please justify:

_____

_____

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7.0 Use of Animal species with Zoonotic Hazards

7.1 Will any of the following animals or their organs, tissues, lavages or other body fluids including blood be used?

- Pound source dogs O YES ~~O~~NO
- Pound source cats O YES ~~O~~NO
- Cattle, sheep or goats O YES ~~O~~NO
- Non-human primates O YES, please specify species _____ ~~O~~NO
- Wild caught animals O YES, please specify species & colony # _____ ~~O~~ NO
- Birds O YES ~~O~~NO
- Others (wild or domestic) O YES, please specify Rabbits ~~O~~NO

8.0 Biological Toxins

8.1 Will toxins of biological origin be used? O YES ~~O~~NO If no, please proceed to Section 9.0

8.2 If YES, please name the toxin(s)_____
Please attach information, such as a Material Safety Data Sheet, for the toxin(s) used.

8.3 What is the LD_{50} (specify species) of the toxin_____

8.4 How much of the toxin is handled at one time*? _____

8.5 How much of the toxin is stored*? _____

8.6 Will any biological toxins be used in live animals? O YES, Please provide detais:_____ O NO

*For information on biosecurity requirements, please see:
http://www.uwo.ca/humanresources/docandform/docs/healthandsafety/biosafety/Biosecurity_Requirements.pdf

9.0 Insects Requiring CFIA Permits

9.1 Do you use insects that require a permit from the CFIA? O YES ~~O~~NO
If no, please proceed to Section 10.0

9.2 If YES, please give the name of the species. _____

9.3 What is the origin of the insect? _____

9.4 What is the life stage of the insect? _____

9.5 What is your intention? O Initiate and maintain colony, give location: _____
O "One-time" use, give location: _____

9.6 Please describe the risk (if any) of escape and how this will be mitigated:
_____
_____
_____

9.7 Please attach the CFIA permit.

9.8 Please describe any CFIA permit conditions:
_____
_____

*** DESCRIPTION MUST BE ATTACHED TO THIS FORM OR PROJECT WILL NOT BE REVIEWED***

10.0 Plants Requiring CFIA Permits

10.1 Do you use plants that require a permit from the CFIA? O YES ~~O~~NO
If no, please proceed to Section 11.0

10.2 If YES, please give the name of the species. _____

10.3 What is the origin of the plant? _____

10.4 What is the form of the plant (seed, seedling, plant, tree...)? _____

10.5 What is your intention? O Grow and maintain a crop O "One-time" use

10.6 Do you do any modifications to the plant? O YES O NO
If yes, please describe: _____
_____

10.7 Please describe the risk (if any) of loss of the material from the lab and how this will be mitigated:
_____
_____
_____

10.8 Is the CFIA permit attached? O YES O NO
If NO, please forward the permit to he Biosafety Officer when available.

10.9 Please describe any CFIA permit conditions:
_____
_____
_____

11.0 Import Requirements

11.1 Will any of the above agents be imported? O YES, please give country of origin_____
If no, please proceed to Section 12.0 ~~O~~NO

11.2 Has an Import Permit been obtained from HC for human pathogens? O YES O NO

11.3 Has an import permit been obtained from CFIA for animal or plant pathogens? O YES O NO

11.4 Has the import permit been sent to OHS? O YES, please provide permit # _____ O NO

12.0 Training Requirements for Personnel Named on Form

All personnel named on the above form who will be using any of the above named agents are required to attend the following training courses given by OHS:

- Biosafety
- Laboratory and Environmental/Waste Management Safety
- WHMIS (Western or equivalent)
- Employee Health and Safety Orientation

As the Principal Investigator, I have ensured that all of the personnel named on the form who will be using any of the biohazardous agents in Sections 1.0 to 9.0 have been trained.

SIGNATURE _____

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13.0 Containment Levels

11.1 For the work described in sections 1.0 to 9.0, please indicate the highest HC or CFIA Containment Level required. O 1 ~~O 2~~ O 3

13.2 Has the facility been certified by OHS for this level of containment?
~~O~~ YES, permit # if on-campus_____.
O NO, please certify
O NOT REQUIRED for Level 1 containment

PHAC certified on July 16, 2008 Jane Ryder

14.0 Procedures to be Followed

14.1 As the Principal Investigator, I will ensure that this project will follow the Western Biosafety Guidelines and Procedures Manual for Containment Level 1 & 2 Laboratories (and the Level 3 Facilities Manual for Level 3 projects). I will ensure that UWO faculty, staff and students working in my laboratory have an up-to-date Hazard Communication Form, found at http://www.wph.uwo.ca/

SIGNATURE _____ Date: Nov 2, 2009

14.2 Please describe additional risk reduction measures will be taken beyond containment level 1, 2, or 3 measures, that are unique to this agent.

My lab is a level 2 certified lab with certified fume hoods and biological safety cabinets, following Health Canada's laboratory biosafety guidelines for handling infectious substances (Chapter 3), with worker training for the specific agent being used, training on universal precautions, personal protective equipment or any administrative or engineering controls.

14.3 Please outline what will be done if there is an exposure to the biohazards listed, such as a needlestick injury:

Follow the Workplace Occurrence Reporting Policy and Procedures, report to OHSS for first aid, complete a workplace occurrence report and cooperate with health care treatment.

15.0 Approvals

UWO Biohazard Subcommittee: SIGNATURE: _____
Date: _____

Safety Officer for Institution where experiments will take place: SIGNATURE: Jane Ryder
Date: November 3, 2009

Safety Officer for University of Western Ontario (if different from above): SIGNATURE: _____
Date: _____

Approval Number: _____ Expiry Date (3 years from Approval): _____

Special Conditions of Approval:

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Cell Biology Collection

Product Description

Before submitting an order you will be asked to read and accept the terms and conditions of ATCC's Material Transfer Agreement or, in certain cases, an MTA specified by the depositing institution.

Customers in Europe, Australia, Canada, China, Hong Kong, India, Japan, Korea, Macau, Mexico, New Zealand, Singapore, and Taiwan, R.O.C. must contact a local distributor for pricing information and to place an order for ATCC cultures and products.

Cell Biology

ATCC® Number:	CRL-1658™ Order this item	**Price:**	$203.00
Designations:	NIH/3T3		
Biosafety Level:	1	**Shipped:**	frozen
Medium & Serum:	See Propagation	**Growth Properties:**	adherent
Organism:	*Mus musculus* (mouse)	**Morphology:**	fibroblast PHOTO
Source:	**Organ:** embryo **Cell type:** fibroblast; fibroblast		
Permits/Forms:	In addition to the MTA mentioned above, other ATCC and/or regulatory permits may be required for the transfer of this ATCC material. Anyone purchasing ATCC material is ultimately responsible for obtaining the permits. Please click here for information regarding the specific requirements for shipment to your location.		

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Cell Biology Collection

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Customers in Europe, Australia, Canada, China, Hong Kong, India, Japan, Korea, Macau, Mexico, New Zealand, Singapore, and Taiwan, R.O.C. must contact a local distributor for pricing information and to place an order for ATCC cultures and products.

Cell Biology

ATCC® Number:	CRL-1435™ Order this item	**Price:**	$203.00
Designations:	PC-3	**Depositors:**	ME Kaighn
Biosafety Level:	1	**Shipped:**	frozen
Medium & Serum:	See Propagation	**Growth Properties:**	adherent(The cells form clusters in soft agar and can be adapted to suspension growth)
Organism:	*Homo sapiens* (human)	**Morphology:**	epithelial PHOTO
Source:	**Organ:** prostate **Disease:** adenocarcinoma **Tumor stage:** grade IV **Derived from metastatic site:** bone		
Permits/Forms:	In addition to the MTA mentioned above, other ATCC and/or regulatory permits may be required for the transfer of this ATCC material. Anyone purchasing ATCC material is ultimately responsible for obtaining the permits. Please click here for information regarding the specific requirements for shipment to your location.		

XUAN, Jim W	PROJECT NO: 07NOV-52

RESUBMISSION DETAILS

LAY SUMMARY

Specific in vivo delivery of drugs is a key goal for all therapies. We propose the first application of UTMD (Ultrasound Targeted Microbubbles Destruction) technology for prostate tissue targeting, molecular diagnosis and therapy in our two genetically engineered mouse prostate cancer models.

Many human diseases, including cancer, are the consequence of multiple factors and multiple consecutive procedures, therapy targeted only on one factor/gene will be less effective than targeting simultaneously to multiple factors. For this purpose, we propose an improved Compound MBs enhanced UTMD (CME-UTMD) strategy, which will enable us to include multiple therapeutic agents in to each targeted microbubble for in vivo delivery simultaneously. Both preventional and interventional therapy targeting to several well studied genes in our laboratory will be performed and monitored by micro- and molecular imaging in our citywide multidisciplinary team.

XUAN, Jim W | PROJECT NO: 07NOV-52

SCIENTIFIC SUMMARY

CaP (prostate cancer) is the most common cancer in adult men in North America. Since there is no naturally occurring CaP in rodents, both basic and preclinical studies employ genetically engineered (GE) mouse with autochthonous CaP. Currently, the most widely used GEM-CaP models all utilize the SV40 Tag oncogene, which demonstrates the complete process of tumorigenesis, tumor progression and metastasis and thereby more accurately recapitulate the biology of human CaP. We have established two PSP94 gene- directed TransGenic (TGMAP, Gene Therapy2002) and Knock In (KI) Mouse Adenocarcinoma Prostate (MAP) (Oncogene 05) models. The knock in model (KIMAP) represents the first application of knock-out mouse technology to generate GEM-CaP.

Specific in vivo delivery of drugs or treatments to tumor tissues is always the key issue for all therapies, including chemotherapy, radiotherapy, surgery, and gene therapy. Currently there is no effective way for tissue specific delivery of chemicals (including RNAi technology) in vivo, we propose the first application of UTMD (Ultrasound Targeted Microbubbles Destruction) technology for precise prostate tissue targeted delivery of therapeutic agents in vivo in animal models. Microbubbles (MBs) are small bubbles constructed of a lipid shell and fill with a biologically inert gas as a contrast agent for imaging. MBs as contrast materials require a small dosage and show excellent detection sensitivity. UTMD takes advantage of the physical properties of MBs to enable in vivo tissue-specific focal release of entrapped materials in the sonification zone, such as oligopeptides, plasmid DNA, siRNA and recombinant viruses, together with the imaging contrast materials, this will result in a technological innovation from the conditional knockout (Cre-LoxP system) in that, the process may take a few seconds to days instead of years.

For molecular diagnosis and prognosis, we propose to use Flk1 (VEGFR2) and CD31 for conjugating of targeted microbubbles for molecular targeted imaging of prostate cancer in both of our TGMAP and KIMAP mice. The application to KIMAP will more closely mimic clinical CaP situation. We have obtained published results as pilot studies in these two genes (Can Res 2005, 2007).

For molecular therapy, we must consider that all human diseases are caused by multiple factors and multiple consecutive procedures, targeted therapy only on one factor/gene will less effective than targeting simultaneously to multiple factors. For this purpose, we propose an improved Compound MBs enhanced UTMD (CME-UTMD) strategy, which will enable us to include multiple therapeutic agents into each targeted microbubble for in vivo delivery. Both preventional and interventional therapy targeting to several well studied genes in our laboratory will be performed and monitored by micro- and molecular imaging in our citywide multidisciplinary team.

Our citywide multi-disciplinary research team consists of molecular biologists, oncologists, urologists, imaging specialists, biophysicists, and pathologists. We have the expertise in micro- and molecular imaging (Can Res 05, 07) and UTMD technology (manuscript in submission) in our GEM-CaP mice. The current proposals will be continuing our current UTMD molecular imaging work with the targeted MBs in our CaP models. Since MBs have been approved by US FDA as type IV contrast agent, we are confident that by developing UTMD technology to interfere SV40Tag oncogene induced tumorigenesis in vivo in our GEM-CaP models, will enable us to develop new strategies for therapies on new tumorigenesis targets in pre- clinical studies of CaP, which would potentially lead to clinical trials.

Subject: Re: Biohazardous Agents Registry Form: Xuan
From: Jim Xuan <Jim.Xuan@LHSC.ON.CA>
Date: Tue, 03 Nov 2009 17:54:46 -0500
To: jstanle2@uwo.ca

Yes. It has been approved exactly as this. -Jim

Jennifer Stanley <jstanle2@uwo.ca> 11/03/09 4:07 PM >>>

Hi Dr. Xuan
I got your completed form by fax today.
It mentions rabbits in Section 7.1 - are these the rabbits used for antibody production (AUS 2008-098)?
Please confirm.
Thanks
Jennifer