

Toya N. Baral, PhD

112 Deercroft Avenue, Nepean, ON, K2J5H7,

Home: 613 440 2324 Work: 613 993 8097

Email: tbaral@yahoo.com, toyanath.baral@nrc-cnrc.gc.ca

Profile:

- Experience in phage display technology, antibody engineering, library construction, affinity maturation.
- Experience of working with human pathogen (human trypanosomes) and as such requiring higher level of Biosafety (BSL3) containment
- Experience in conducting pre-clinical experiments for evaluation of biologics for their therapeutic as well as diagnostic application.
- Experience in writing, publishing and reviewing scientific papers
- Ability to work in different projects, under tight deadlines and in different environments
- Ability to collect, analyze and synthesize information from different sources and make evidence based recommendations
- Able to communicate effectively orally and in writing
- Knowledge of general molecular biology, immunology, pathology, toxicology and drug pharmacokinetics.
- Knowledge of pathological techniques such as immunohistochemistry, histology, immunofluorescence.
- Knowledge of theories and principles of host pathogen interaction, host immune response, immunopathology
- Knowledge of biology, current diagnostic and therapeutic approaches of cancer
- Knowledge of infectious diseases such as trypanosomes and influenza

Professional experience:

- **Research Associate** 2007 to present
- **Postdoctoral Researcher** 2006 to 2007
National Research Council of Canada
Institute of Biological Sciences, Ottawa, Canada
 1. Working in generation of "ideal" single domain antibody for the therapeutic or diagnostic application for cancer as well as infectious diseases
 2. Isolated single domain antibody against breast cancer, pancreatic cancer as well as against influenza virus
 3. Modified/engineered these antibodies tailored/conjugated with effectors molecules such as Fc, cytokines or radiolabelled them or conjugated them with quantum dots (in collaboration). The quantum dots conjugated antibodies were used for immunofluorescence study.
 4. Conducted in vitro as well as in vivo experiments to evaluate the potential of these antibodies as therapeutic diagnostic application against breast and pancreatic cancer or influenza virus.
 5. Studied serum half life, tumor retention time, bio-distribution of some of these antibodies or their derivatives
 6. Co-authored 8 manuscripts with significant contribution in preparing and reviewing them.
 7. Wrote 2 grants applications, one for Bill and Melinda Gates Foundation and another for National Institute of Health (NIH).
 8. Writing as well as presenting in several internal as well as external meetings/seminars/conferences
 9. Worked as a peer reviewer for the journal "Trends in Parasitology"

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10. Provided partial guidance to a postdoc fellow as well as supervise undergraduate student.

- **Graduate (Ph.D.) Research** 2001-2006
- **Graduate student (MSc)** 1999-2001
Vrije University of Brussels, Belgium
 1. Developed alternative approaches for the treatment as well vaccination against trypanosome; a human as well animal pathogen. For the human pathogenic trypanosomes the work was conducted in higher level of biosafety containment. The study included several pathological aspects of the diseases as well as some microscopic analysis of results.
 2. Designed, engineered different molecules for their potential as alternative treatment or vaccination tools.
 3. Conducted different in vitro as well as in vivo experiments that include the challenge experiments, survival analysis, toxicological analysis, bio-distribution of the biological drug.
 4. Studied immune-pathological aspect of the trypanosomiasis
 5. Collected results analyzed and prepared scientific manuscripts.
 6. Authored 3 papers as first and corresponding author, including one published in the journal "Nature Medicine" and co-authored 5 papers in peer reviewed journals.
 7. Prepared and presented scientific results in different national as well as international conferences
- **Lecturer, 1996 to 1999_Tribhuvan University, Nepal**
 1. Teaching to the undergraduate student of veterinary school.
 2. Involved in research activities internally funded by the Directorate of Research of the university.

Education:

PhD (Immunology, Applied Biological Sciences), Vrije University of Brussels, Belgium. Major: Molecular Biology, Biochemistry and Immunology. **Dissertation title** "*Development of alternative strategies for control of human and livestock trypanosomiasis.*"

M.Sc. in Molecular Biology, Vrije University of Brussels, Belgium. Major: Molecular Biology, Pharmacology, Pathology, Immunology, Physiology. **Dissertation title:** "*Development of anti-disease vaccine against African trypanosomiasis.*"

Language Proficiency:

Excellent: English, Nepali and Hindi

Basic (Speaking, listening and writing): French

Patents:

1. WO/2010/043053) Single domain antibody functionilzed Quntum dots for cellular imaging of cancer cells. International application number: **PCT/CA2009/001490**
2. Anti-CEACAM Antibodies and Uses Thereof: US Provisional Appln No. 61/388,746

Publications:

1. **Toya Nath Baral**, Yanal Murad, Than Dung Nguyen, Umar Iqbal and Jianbing Zhang. Isolation of functional single domain antibody by whole cell immunization: application in cancer. *Journal of Immunological Methods*. 2011, 231: 70-80.

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2. **Toya Nath Baral**. Immunobiology of African trypanosomes: need of alternative interventions. *Journal of Biomedicine and Biotechnology*. 2010; 2010:389153.
3. **Toya Nath Baral**, Mehdi Arbabi-Ghahroudi. Expression of Single-Domain Antibodies in Bacterial Systems. In press in *Methods in Molecular Biology*.
4. Md. Badruz Zaman, **Toya Nath Baral**, Zygmunt J. Jakubek, Jianbing Zhang, Edward Lai, Dennis Whitfield, and Kui Yu. Single-Domain Antibody Bioconjugated Near-IR Quantum Dots for Targeted Cellular Imaging of Pancreatic Cancer. *Journal of Nanomedicine and Nanotechnology*. 2011, 11: 3757-3763.
5. Andrea Bell, Zheng J. Wang, Mehdi Arbabi, Anthony T. Chang, Yves Durocher, Ulrike Trojahn, Jason Baardsnes, Maria L. Jaramillo, Shenghua Li, **Toya Nath Baral**, Maureen O'Connor-McCourt, Roger MacKenzie and Jianbing Zhang. Differential tumor-targeting abilities of three single-domain antibody formats. *Cancer Letter* 2010, 289(1):81-90.
6. Serge Muyldermans, **Toya Nath Baral**, V. Cortez Retamozzo, P. De Baetselier, E. De Genst, J. Kinne, H. Leonhardt, S. Magez, V.K. Nguyen, H. Revets, U. Rothbauer, B. Stijlemans, S. Tillib, U. Wernery, L. Wyns, Gh. Hassanzadeh-Ghassabeh and Dirk Saerens. Camelid immunoglobulins and nanobody technology. *Veterinary Immunology and Immunopathology*. 2009, 128: 178-183
7. Md Badruz Zaman, **Toya Nath Baral**, Dennis Whitefield, Jianbing Zhang and Kui Yu. Single Domain Antibody Functionalized CdSe/ZnS Quantum Dots for Cellular Imaging of Cancer Cells. *Journal of Chemical Physics* 2009, 113 (2) :496-499
8. Jianbing Zhang, Xin Lui, Andrea Bell, Rebecca To, **Toya Nath Baral**, Ali Azizi, Jianjun Li, Brian Cass and Yves Durocher. Construction and characterization of chimeric heavy chain antibodies (Submitted to *Protein Engineering, Design, and Selection* 2009, May 65(1):77-82
9. Dirk Saerens, Benoît Stijlemans, **Toya Nath Baral**, Nguyen Thi Giang Thanh, Kinne Joerg, Patrick De Baetselier, Stefan Magez, Serge Muyldermans and Katja Conratha. Parallel selection of multiple anti-infectom Nanobodies without access to purified antigens. *Journal of Immunological Methods* 2008 Jan 1; 329(1-2):138-50.
10. Stefan Magez, Magdalena Radwanska, Michael Drenan, Lizette Fick, **Toya Nath Baral**, Nasiema Allie, Muazzam Jacobs, Sergei Nedospasov, Frank Brombacher Bernard Ryffel, and Patrick De Baetselier. TNFp55 signal transduction and macrophage derived soluble TNF are crucial for nitric oxide mediated *T. congolense* parasite killing. *Journal of Infectious Diseases* 2007, Sep 15;196(6):954-62.
11. Benoît Stijlemans, **Toya Nath Baral**, Martin Williams, Lea Brys, Johanna Korf, Michael Drennan, Jan Van Den Abbeele, Patrick De Baetselier and Stefan Magez. A Glycylphosphatidylinositol-Based treatment alleviates trypanosomiasis-associated immunopathology. *Journal of Immunology*. 2007. 179: 4003-4014 / No. 6 / Sep 15, 2007
12. **Toya Nath Baral**, Frank Brombacher, Patrick De Baetselier and Stefan Magez. Control of *Trypanosoma evansi* infection is IgM mediated and does not require a classical type I inflammatory response. *Journal of Infectious Diseases*. 2007 May 15;195(10):1513-20
13. **Toya Nath Baral**, Stefan Magez, Benoît Stijlemans, Katja Conrath, Benoit vanhollebeke, Etienne Pays, Serge Muyldermans and Patrick De Baetselier. Experimental therapy of African trypanosomiasis with a nanobody-conjugated human trypanolytic factor. *Medicine Science (Paris)*. 2006 Nov; 22(11):914-6. French
14. **Toya Nath Baral**, Stefan Magez, Benoît Stijlemans, Katja Conrath, Benoit vanhollebeke, Etienne Pays, Serge Muyldermans and Patrick De Baetselier. Experimental therapy of African trypanosomiasis with a nanobody-conjugated human trypanolytic factor. *Nature Medicine*. 2006 May;12(5):580-4.
15. Stefan Magez, Magdalena Radwanska, Michael Drenan, Lizette Fick, **Toya Nath Baral**, Frank Brombacher and Patrick De Baetselier. INF γ and NO in combination with

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- antibodies are key protective host immune factors during *T. congolense* TC13 infections. *Journal of Infectious Diseases*. 2006, 1;193(11):1575-1583
16. Stefan Magez, Benoît Stijlemans, **Toya Nath Baral**, Patrick De Baetselier. VSG-GPI anchors of African trypanosomes: their role in macrophage activation and induction of infection-associated immunopathology. *Microbes Infect.* 2002, 4:999-1006

Manuscripts submitted/ in preparation:

1. Bin Mu, Tomoko Hirama, Shenghua Li, **Toya Nath Baral** and Jianbing Zhang , Fast screening of expression levels, biophysical properties and affinities of a large number of proteins (Under review in PEDS)
2. **Toya Nath Baral**, Shi-yu Chao, Shenghua Li, Jamshid Tanha, Mehdi Arbabi-Ghahroudi, Shu-ying Sherry Wang, Jianbing Zhang. Crystal structure of a dimeric anti-HER2 single domain antibody (Submitted to Journal Molecular Biology)
3. **Toya Nath Baral**, Henk van Faassen, Jianbing Zhang, Screening of Expression Levels by Surface Plasmon Resonance with the Help of a Novel Protein Tag (manuscript in preparation)
4. Tsai-Mu Cheng, Yanal M. Murad, Chia-Ching Chang, Ming-Chi Yang, **Toya Nath Baral**, Aaron Cowan, Shin-Hua Tseng, Roger MacKenzie, Jianbing Zhang. Single domain antibody against CEACAM6 inhibits proliferation migration, invasion, and angiogenesis of pancreatic cancer cells. Submitted to Cancer Research.
5. **Toya Nath Baral**, Jason Baardsnes, Henk van Faassen, Shenghua Li, Maureen O'Connor-McCourt and Jianbing Zhang, Isolation of functional single domain antibody against CEACAM6 (Manuscript in preparation).

Book:

- Alternative strategies for control of Trypanosomiasis, 2010, Lap Lambert Academic Publishing Ag & Co. ISBN: 3838367987

Oral presentations:

- 1) Single domain antibodies as therapeutic candidates against cancer and infectious diseases, Institute of Biological Sciences, Ottawa, May 7, 2008
- 2) Single domain antibody against HER2, in the view of breast cancer diagnosis and therapy, Biotechnology Research Institute, Montreal, February 25, 2008
- 3) Transmission, Immunology and Treatment of African Trypanosomiasis. VIB Seminar, Blankenberg, March 9-10, 2006
- 4) Nanobody as targeting tool for human trypanolytic factor (apoL-I). Annual meeting of OIE ad hoc group on Non Tsetse Transmitted Animal Trypanosomes (NTTAT), 22 May 2005. Paris, France
- 5) Nanobody as targeting tool for human trypanolytic factor (apoL-I). Annual meeting of Belgian Protozoology society, February 2005. Antwerp, Belgium
- 6) Nanobody as targeting tool for human trypanolytic factor (apoL-I).Workshop of South Africa-Flanders Bilateral Programme on "Host-trypanosome intereaction.28-29 October, 2004. Antwerp, Belgium
- 7) Nanobody as targeting tool for human trypanolytic factor (apoL-I). A meeting involving all participants of the Inter University Attraction pole (IUAP) program, 6 October 2004.VUB, Brussels. Belgium
- 8) Efficient trypanosomiasis therapy with nanobody conjugated human trypanolytic factor, Drug Development for parasitic diseases, 1st COST B 22 congress, 22-24 November 2004, Antwerp, Belgium.

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Poster presentations:

- 1) Human single domain and fully human heavy chain antibodies against HER2; 9th Annual General Meeting of Genome and Health Initiatives, National Research Council of Canada, Montreal, 2009 June 8-10
- 2) GPI-based vaccine strategy as a candidate to prevent infection associated immune complications during experimental trypanosome infections; Eighth Annual Woods Hole Immuno Parasitology Conference, April 25-28, 2004
- 3) Efficient trypanosomiasis therapy with nanobody conjugated human trypanolytic factor, British Society for Parasitology, Trypanosomiasis and leishmaniasis Seminar, Ceske Budejovice, August 27-30, 2004.
- 4) GPI-based vaccine strategy as a candidate to prevent infection associated immune complications during experimental trypanosome infections. British Society for Parasitology, Trypanosomiasis and leishmaniasis Seminar, Ceske Budejovice, August 27-30, 2004.
- 5) Transmission, Immunology and Treatment of African Trypanosomiasis. VIB Seminar, Blankenberg, March 3-4, 2005.
- 6) Transmission, Immunology and Treatment of African Trypanosomiasis. Follow-up Meeting for IPMB Programme. August 22-27, 2005. Brussels
- 7) Experimental therapy of African trypanosomiasis with a nanobody-conjugated human trypanolytic factor. Tenth Annual Woods Hole Immuno Parasitology Conference, 2006

Honours and Scholarships:

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| 2007 | Development co-operation Prize by Belgian Government as a young researcher for the contribution in developing world. |
| 2006-2007 | Natural Sciences and Engineering Research Council postdoc fellowship to work as postdoc in National Research Council of Canada (NRC) in Institute of Biological Sciences. |
| 2001-2006 | Free University of Brussels' Special Research Fund Scholarship to pursue Ph.D. in Belgium. |
| 1999-2001 | Flemish Interuniversity Council Scholarship to pursue M.Sc. in Molecular Biology in Belgium. |
| 1988-1994 | University talent scholarships during Bachelor in Veterinary Science in Nepal. |

Scientific skills:

- Construction of single domain antibody library, phage display and bio-panning
- Basic techniques of tumor cell line maintenance and in vitro experiments with tumor cells
- In vivo animal experiments with different tumor model.
- Microscopy, immunofluorescence, immunohistochemistry
- Affinity measurement and epitope mapping of antibody.
- Basic technique of antibody engineering.
- Fractionation of serum for different sub-classes of IgGs
- Iso-type analysis of antibody response.
- Both normal and sandwich ELISA.
- Maintenance, infection and purification of different trypanosomes.
- *In vitro* culture of trypanosomes.
- *In vivo* immunization, challenge and treatment of mice for trypanosomiasis.
- Experience with different injection routes in mice (intramuscular, subcutaneous, intraperitoneal, and intravenous).
- Dissection of various mouse organs

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- Splenectomy operation of mouse.
- Isolation of mouse peritoneal exudates cells (PECS), splenocytes, liver cells, lymphnode cells.
- Mammalian cell culture, cytokines measurement and analysis.
- Cell proliferation assays and analysis.
- Purification of RNA, cDNA synthesis, normal and real-time PCRs for both qualitative as well as quantitative analysis.
- Differential gene expression analysis.
- FACS analysis.
- Construction of VHH library from the cDNA, phage display and bio-panning.
- Restriction Fragment Length Polymorphism (RFLP)
- SDS-PAGE, Western Blotting, Immunoprecipitation and Immunofluorescence microscopy. Cloning, expression and purification of recombinant proteins in bacteria, yeast and mammalian expression system.
- HPLC and FPLC for protein purification.
- Fractionation of serum for different sub-classes of IgGs
- Iso-type analysis of antibody response.
- Both normal and sandwich ELISA.