

## BIOGRAPHICAL SKETCH

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NAME <b>Maria Contel</b>		POSITION TITLE <b>Professor</b>	
eRA COMMONS USER NAME <b>MCONTEL</b>		<b>Inorganic Chemistry</b> <b>Brooklyn College, CUNY</b>	
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
University of Zaragoza (Spain)	BSc/MSc	1993	Chemical Sciences, Inorganic Chemistry
Public University of Navarra (Spain)	Ph.D	1996	Chemistry
Australian National University (Australia)	Postdoc	1997-1999	Organometallics
University of Utrecht (The Netherlands)	Postdoc	1999-2000	Organometallics
University of Zaragoza-CSIC (Spain)	Senior Researcher	2001-2006	Homogeneous Catalysis
HERS Institute (USA)	Leadership Certificate	2018	Higher Education

### A. PERSONAL STATEMENT

#### Research and mentoring qualifications

My research program focuses on the synthesis and characterization of transition-metal complexes (mainly gold but also titanium, silver, copper, palladium and platinum) and their applications as: a) anticancer and antimicrobial agents and b) as catalysts in reactions of industrial interest (including but not limited to oxidations and C-C and C-Heteroatom bond formation). After working on synthetic organometallic chemistry and homogeneous catalysis for years, I transitioned in 2008 to the field of medicinal inorganic chemistry. My first NIH funded research (SC2 award, Feb 2010-June 2013) focused on the preparation of gold compounds with phosphorous-containing pincer ligands as potential anticancer agents. The long-term goal of my research is the development of novel metal-based anticancer chemotherapeutics that can overcome some of the drawbacks associated with the use of platinum drugs. More recently (since 2011) we have focused on the preparation of heterometallic gold complexes (compounds containing a second metal besides gold) as anticancer and as antimicrobial agents. Our hypothesis is that the incorporation of two different metals with anti-tumor properties in the same molecule will improve their activity due to: a) interaction of the different metals with multiple biological targets and b) improved chemico-physical properties of the resulting heterometallic compound. In this context we have reported that such an approach is a feasible one and that new titanium-gold complexes may be promising candidates with improved antitumor properties with respect to their monometallic (titanium and gold) precursors in different cancers (*Inorg. Chem.* 2011). These studies formed the preliminary data for an NIH-SC1 proposal (July 2013-June 2017) and now we have data for the real potential of these derivatives in renal and prostate cancer (*Organometallics* 2014, 2016, *Eur. J. Med. Chem.* 2019) including relevant *in vivo* work in mice (*Chem. Sci.* 2015, US patent 2016 and unpublished data in collaboration with Dr. Hubbard 2019). We have extended our work to include ruthenium-gold derivatives with improved anticancer profiles (*Dalton Trans.* 2015, *Chem. Commun.* 2016, *J. Inorg. Biol. Chem.* 2018 and *Cancer Medicine* 2019 in collaboration with Dr. Hubbard, 2019). In addition to being a faculty member at the Chemistry PhD program at the Graduate Center in CUNY, I am a faculty member of the Biology PhD Program since 2015 and of the Biochemistry PhD program in 2018.

In my research group, we have also performed research on the topic of *ruthenium compounds as anti-cancer* and thus we published and patented work on ruthenium-based organometallic compounds

highly effective in vitro and in vivo against triple negative breast cancer (*J. Med. Chem.* 2014, US patent 2017) and on dendrimers incorporating organometallic ruthenium compounds as anticancer agents (*Dalton Trans* 2016). During my career I have published over 60 articles on the synthesis and applications of organometallic and coordination complexes from different transition metals. I am also currently working on new “vehicles” for a better delivery of metallodrugs in order to generate safer and more selective “targeted” cancer chemotherapeutics. We have a project on the incorporation of different active metal-based anticancer drugs into biodegradable enzyme-specific cleavable nanocarriers to improve the delivery and release in the specific tumor site. We also have a breast cancer project (targeted therapies) for breast cancers overexpressing HER-2 in which we are preparing novel antibody drug conjugates by bio-conjugation of 2 highly cytotoxic gold compounds to the monoclonal antibody trastuzumab (Herceptin®). This project is in collaboration with Memorial Sloan Kettering Cancer Center. This last two projects have been funded by a grant from NIH (SC1) for the period June 2018-June 2022. These projects do not overlapped with the project presented in this proposal.

Since I joined Brooklyn College in 2006 I have supervised 5 research associates, 7 graduate (4 PhD), 35 undergraduate and 3 high school students, with over 75% of them coming from groups underrepresented in chemistry (minority students, females and persons with disabilities) including MARC and LSAMP students. Many of the undergraduate students were co-authors in publications and 7 of these students joined PhD programs in biomedical areas (chemistry, biochemistry and biology) or sciences (mathematics) while most of the others went to medical schools. I have also supervised 5 students from foreign universities who have done either a masters or a PhD research stay in my group. I am currently the mentor of Prof. Guillermo Gerona-Navarro, an Assistant Professor at the Chemistry Department of Brooklyn College for his SCORE SC2 application which was awarded in 2014. I am also part of the mentoring team for Prof. Mariana Torrente, an Assistant Professor at the Chemistry Department of Brooklyn College who joined BC in August 2015 and who is a holder of a K22 award from NIH.

I am a regular reviewer for a variety of prestigious journals in chemistry and medicinal chemistry and a regular reviewer of NSF and PRF grants (including panels) and of some grants from other countries (such as Hong Kong Council Review, Czech Republic Science Ministry, National Research Foundation (NRF) of South Africa or the Israel Science Foundation) in the areas of medicinal inorganic chemistry, organometallic chemistry and homogeneous catalysis.

## B. POSITIONS AND HONORS

### Positions and Employment

**1997-1999 Postdoctoral Fellow.** *Subject:* Synthesis of organometallic compounds with bridging  $C_6H_4PR_2$  (R = Ph, Et) ligands. *Location:* Research School of Chemistry, Australian National University, Australia. *Supervisor:* Prof. Martin A. Bennett.

**1999-2000 Postdoctoral Fellow.** *Subject:* Synthesis of orthometallated gold compounds with NCN ligands. *Location:* Metal-Mediated Organic Synthesis Department. Debye Institute. University of Utrecht. The Netherlands. *Supervisor:* Prof. Gerard van Koten.

**2000-2001 Research Associate.** Funded by the Spanish Ministry of Science and Education and CSIC. *Subject:* Complexes with polyfunctional thiolates. *Location:* Materials Science Institute of Aragón, Zaragoza. *Advisor:* Prof. Mariano Laguna.

**2002-2006 Senior Research Contract “Ramón y Cajal”.** Spanish Ministry of Science and Education. 5-year Senior Research Position. *Subject:* Compounds of groups 10 and 11 metals as recyclable catalysts for carbon-carbon and carbon-heteroatom bond formations. *Location:* Inorganic Chemistry Department, University of Zaragoza. Spain.

**2006-2010 Assistant Professor (Inorganic Chemistry).** Chemistry Department, Brooklyn College and The Graduate Center, City University of New York (CUNY).

**2014 Fall- Present Faculty, Biology PhD Program, The Graduate Center, CUNY**

**JAN 2011-August 2016 Associate Professor (Inorganic Chemistry).** Tenured in August 2011. Chemistry Department, Brooklyn College and The Graduate Center, CUNY.

**August 2016-Present Professor (Inorganic Chemistry).** Chemistry Department, Brooklyn College, CUNY.

**July 2017-Present Chairperson.** Chemistry Department, Brooklyn College, CUNY.

**2018 Spring- Present Faculty, Biochemistry PhD Program,** The Graduate Center, CUNY

### Honors and Awards

**2018** Don Quijote Leadership Award. Puerto Rican and Latino Studies Department at Brooklyn College & Puerto Rican Alliance.

**2018** HERS-Leadership Training Institutes for Women in Higher Education Summer 2018 CBL STEM Fellowship (to attend the two week institute in July of 2018, Bryn Mawr College, PA)

**2018** Schwartzman, George and Beatrice Professor in Chemistry (Brooklyn College).

**2015-2017** Tow Professor (at Brooklyn College). Highest recognition in research from Brooklyn College.

**2014-Present** Associate and Full Member of the University of Hawaii Cancer Center (Cancer Biology Program, Natural Products and Experimental Therapeutics).

**2013** Tow Travel Faculty Fellowship (Brooklyn College). To perform a research stay during the Fall 2013-Spring 2014 academic year at the University of Hawaii-Cancer Center.

**2007** Project Kaleidoscope Faculty Fellow for the 21st Century (PKAL F21) Class of 2007.

**2006** Prominent Research Career Report (I3 Program): Positive Evaluation. ANEP, Spanish National Agency of Evaluation and Prospective.

**2002-2006** Ramon y Cajal Senior Research Position. Most prestigious Spanish Research Fellowship for Young Investigators.

**2005** Teaching Competence Certification (certification to be a University Assistant/Associate Professor in the area of Inorganic Chemistry). ANECA, Spanish National Agency of Evaluation and Academic Certifications.

### C. CONTRIBUTION TO SCIENCE

66 peer reviewed articles (including 2 reviews, 3 book chapters, and a book review), 2 patents issued and one filed in 2018, over eighty communications or invited talks at National and International Conferences. One article submitted and three articles in preparation for submission in 2019.

1) **Gold homo and heteronuclear compounds and clusters** (PhD studies. Advisors: Prof. Laguna and Prof. Garrido). From the results obtained during my PhD, I published 10 papers. My work dealt with the preparation of novel polynuclear gold complexes to study the formation of supported and unsupported Au-Au and Au-M (Ag, Cu, Sn, Ge) bonds and interactions. These studies were relevant at the time since the effects of aurophilicity were starting to be described in the literature. The aurophilicity (due to relativistic effects) make gold and gold compounds quite unique in their chemical reactivity and have allowed for the explanation of their unexpected behavior in some catalytic processes. My two selected publications are:

- Trinuclear Au<sub>2</sub>Ag and Au<sub>2</sub>Cu Complexes with Mesityl Bridging Ligands. X-Ray Structure of the One-dimensional Chain Polymer [ $\text{Au}(\mu\text{-mes})(\text{AsPh}_3)_2\text{Ag}]\text{ClO}_4$ . **Contel, M.**; Garrido, J.; Gimeno, M.C.; Jones, P.G.; Laguna, A.; Laguna, M. *Organometallics*, **1996**, *15*, 4939.

- 'A New, Simple Route to Novel Gold Clusters: Structure of an Au<sub>6</sub>Ag Wheel with a Gold Rim'. Cerrada, E.; **Contel, M.**; Valencia, A.D.; Laguna, M.; Gelbrich, T.; Hursthouse, M.B. *Angew. Chem. Int. Ed.*, **2000**, *39*, 2353.

2) **Organometallic compounds with pincer P-C and N-C-N ligands** (Postdoctoral Studies). In my first position (Advisor Prof. Bennett), I prepared mono and polynuclear organomercury complexes containing palladium and platinum and was able to assess and describe bonds and interactions Hg-Pd and Hg-Pt. I

used and developed  $^{199}\text{Hg}$  NMR spectroscopy to study such interactions. I also used the organomercury compounds to cleanly transfer the organic groups to Pt, Ru and Os centers. My second postdoctoral position (Advisor Prof. van Koten) dealt with the preparation of gold compounds with N-C-N ligands in different oxidation states. My main achievement in this period was to discover the ability of  $[\text{AuPPh}_3]^+$  fragments to act as  $\text{Li}^+$  or  $\text{MgBr}^-$  equivalents (based on the isolobality of  $\text{AuPPh}_3^+$  and  $\text{H}^+$  and  $\text{Li}^+$ ). In this way I was able to use R-Au-PPh<sub>3</sub> compounds as transmetallating agents to different metallic centers ( $\text{Au}^{\text{III}}$ ,  $\text{Pt}^{\text{II}}$ ,  $\text{Pd}^{\text{II}}$ ,  $\text{Ni}^{\text{II}}$ ,  $\text{Fe}^{\text{III}}$ , and  $\text{Ti}^{\text{IV}}$ ). This is an air stable alternative to lithiated and Grignard reagents when these compounds cannot be used due to the problem of reduction of the metallic centers. It is also a much less toxic alternative to organomercury reagents and a step forward in Green Chemistry. These two positions rendered 5 publications and I was invited to talk at the XVIIIth International Conference on Organometallic Chemistry (Munich, 1998, the most prestigious Conference in the field). My two selected publications are:

- 'Bis{2-diphenylphosphino)phenyl}mercury: a novel bidentate ligand and transfer reagent for the o-C<sub>6</sub>H<sub>4</sub>PPh<sub>2</sub> group'. Bennett, M.A.; **Contel, M.**; Hockless, D.C.R.; Welling, L.L. *Chem. Commun.*, **1998**, 2401.
- 'A Bis(ortho-amine)aryl-Gold(I) Compound as an Efficient, Nontoxic, Arylating Reagent'. **Contel, M.**; Stol, M.; Casado, M.A.; van Klink, G.P.M.; Ellis, D.D.; Spek, A.L.; van Koten, G. *Organometallics*, **2002**, *21*, 4556.

**3) Gold complexes in homogenous catalysis** (Senior Researcher UZ, Assistant/Associate Professor at BC). After my postdoctoral studies I returned to Spain and I worked as a Research Scientist at the University of Zaragoza-CSIC (Department of Inorganic Chemistry). I was awarded a Ramon y Cajal Fellowship in 2002, the most prestigious 5-year fellowship in Spain for young investigators (we could not apply for our own research funds to Federal Agencies and thus had to work with an established PI). I continued with this topic when I first arrived at Brooklyn College and published 8 articles (6 as PI or co-PI). At the time I started the project in 2003 there were only 5 publications (3 very old) of gold homogeneously-catalyzed processes. I focused on establishing reaction mechanisms by *in situ* spectroscopic techniques (mainly NMR). I studied different reactions such as: addition of water and alcohols to alkynes, formation of C-C and C-heteroatom bonds and hydrosilylation. My first piece of work in the field (with undergraduate students R. Casado and S. Sanz) was accepted as a full paper in *J. Am. Chem. Soc.* highly cited in the field (over 310 citations).

- 'Organometallic Gold(III) Compounds as catalysts for the Addition of Water and Methanol to Terminal Alkynes'. Casado, R.; **Contel, M.**; Laguna, M.; Romero, P.; Sanz, S. *J. Am. Chem. Soc.* **2003**, *125*, 11925.
- 'Mechanistic Insights in the One-Pot Synthesis of Propargylamines from Terminal Alkynes and Amines in Chlorinated Solvents Catalyzed by Gold Compounds and Nanoparticles'. Aguilar, D.; **Contel, M.**; Urriolabeitia, E.P. *Chem., A Eur. J.* **2010**, *16*, 9287.

**4) Green chemistry: recyclable catalysts** (Senior Researcher UZ, Assistant/Associate Professor at BC). I published 6 papers, and 2 book chapters all as PI or co-PI. I worked in: 1) the preparation of recyclable fluororous copper compounds as catalysts for the oxidation of alkenes, alkanes and alcohols, and 2) recyclable gold compounds in reactions of hydrosilylation, oxidation and the formation of C-C bonds. The copper catalysts proved to be very efficient (and in some cases with just air or O<sub>2</sub> as oxidizing agents) and could be recycled and re-used without much loss of catalytic activity. We were also able to study the reaction mechanisms by *in situ* EPR spectroscopy. Subsequent work allowed for the preparation of recyclable fluororous copper compounds with thermomorphic properties which permitted their use in oxidation catalysis without fluororous solvents. One selected publication below:

- 'Fluororous Biphasic Catalysis: Synthesis and Characterization of Copper(I) and Copper(II) Fluoropyonytailed 1,4,7-Rf-TACN and 2,2'-Bipyridine Complexes and Demonstration of their Catalytic Activity in the Oxidation of Hydrocarbons, Olefins, and Alcohols, Including Mechanistic Implications'. **Contel, M.**; Izuel, C.; Fish, R.; Laguna, M.; Villuendas, P.R.; Alonso, P.J. *Chem. A. Eur. J.* **2003**, *9*, 4168.

**5) Metallodrugs as antimicrobial and anticancer agents.** I have worked in this field at Brooklyn College since 2009 funded by NIH (NIGMS SC2 grant 2010-2013, NCI S1 grant 2013-2017, NIGMS SC1 grant 2018-2022). More recently my group has reported on the *in vivo* studies of selected compounds (ruthenium, gold-titanocene- and ruthenium-gold-based derivatives) on breast and renal cancer with impressive tumor

reductions or growth inhibition and improved pharmacological profiles. More specifically the ruthenium derivative (a cheap, low molecular weight compound, water soluble and with low toxicity *in vivo*) was able to reduce the tumor size of MDA-MB 231 xenografts in mice in 56 %. This makes it the best ruthenium compound reported so far for triple negative breast cancer. The work on the highly active titanocene-gold derivative on renal cancer represents the first *in vivo* study of a heterometallic anticancer compound along with the best results obtained on renal cancer for a metal-based drug. I have published 25 papers on this topic and a chapter of book since 2009, and I have two patents recently issued and one preliminary filed. I have also published 5 papers in the area of antimicrobial metallodrugs. I have been invited to talk at different International Conferences (including a keynote lecture at the most important conference on my field, the “18<sup>th</sup> International Conference on Biological Inorganic Chemistry, ICBIC 18” Brazil, July 31<sup>st</sup>-August 4<sup>th</sup> of 2017). Importantly, I was the organizer and co-Chair of the ‘1<sup>st</sup> International Symposium on Clinical and Experimental Metallodrugs in Medicine: Cancer Chemotherapy’ held in Honolulu (December 12<sup>th</sup>-15<sup>th</sup>, 2015, <http://cemm.brooklyn.cuny.edu/>) and partly funded by a R13 grant. I was discussion leader in the session of “Recent Developments in Metallodrugs” (Gordon Conference on Metals in Medicine, June 2018). Three more recent selected publications and one issued patent are:

- ‘Arene Ruthenium(II) Derivatives Containing Iminophosphorane Ligands and Their Use in Cancer Therapy’. **Contel, M.**; Marzo, I.; Frik, M.; Elie, B.T. US Patent 9,555,049 B2 (01/31/2017).
- ‘Preclinical Evaluation of an Unconventional Ruthenium-Gold-Based Chemotherapeutic: RANCE-1, in Clear Cell Renal Cell Carcinoma’. Elie, B.T.; Hubbard, K.; Pecheny, Y.; Layek, B.; Prabha, S.; **Contel, M.** Cancer Medicine. Accepted for publication on May, 17, 2109.
- ‘Trastuzumab gold-conjugates: synthetic approach and *in vitro* evaluation of anticancer activities in breast cancer cell lines’. Curado, N.; Dewaele-Le Roi, G.; Poty, S.; Lewis, J.S.; **Contel, M.** *Chem. Commun.* **2019**, 55, 1394-1397.
- ‘Customizing Morphology, Size, and Response Kinetics of Matrix Metalloproteinase-Responsive Nanostructures by Systematic Peptide Design’. Son, J.; Kalafatovic, D.; Kumar, M.; Yoo, B.; Cornejo, M.A.; **Contel, M.**; Ulijn, R.V. *ACS Nano*. **2019**, 13, 1555–1562

List of Published Work in MyBibliography (unfinished):

<http://www.ncbi.nlm.nih.gov/myncbi/browse/collection/47997971/>

## D. RESEARCH SUPPORT

### Ongoing Research support

NIH/NIGMS 2SC1GM127278-05A1	Contel (PI)	06/01/18-05/31/2022
<b>Biodegradable nanocarriers and antibodies as targeting delivery vehicles for cancer metallodrugs</b>		\$1,570,000

### Completed Research Support (Last five years)

NIH/NCI 1SC1CA182844-03	Contel (PI)	07/01/13-05/31/2018
<b>Titanium-gold-based chemotherapeutics for prostate and kidney cancer</b>		\$1,413,000
CUNY-Advanced Science Research Center (SEED grants)	Contel (PI)	06/01/15-05/31/2016
<b>Improving selectivity and delivery of potential organometallic-based cancer chemotherapeutics by using peptide- and carbohydrate- amphiphiles as mobile nanocarriers</b>		\$10000
Tow Foundation	Contel (PI)	06/01/15-05/30/2017
<b>Tow Professor 2015-2017</b>		\$25000 (for research)
NIH/NCI 1R13CA200223-01A1	Contel(PI)	09/01/2015-05/31/2016
<b>Organization Conferences: 1st International Symposium on Clinical and Experimental Metallodrugs in Medicine: Cancer Chemotherapy (CEMM). Honolulu (UHCC) December 2015</b>		\$5000
NIH/NIGM SC2GM082307	Contel (PI)	02/01/10-06/30/2013
<b>Organogold phosphorus-containing compounds as anticancer agents</b>		\$471,000