BIOGRAPHICAL SKETCH

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NAME: Maria Contel

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POSITION TITLE: Professor, Inorganic Chemistry, Brooklyn College, CUNY

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Zaragoza (Spain)	BSc/MSc	06/1993	Chemical Sciences, Inorganic Chemistry
Public University of Navarra (Spain)	Ph.D	07/1996	Chemistry
Australian National University (Australia)	Postdoc	03/1999	Organometallics
University of Utrecht (The Netherlands)	Postdoc	01/2000	Organometallics
University of Zaragoza-CSIC (Spain)	Senior Researcher	06/2006	Homogeneous Catalysis
HERS Institute (USA)	Leadership Certificate	07/2018	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: anticancer and antimicrobial agents. 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). Funded by an NIH-SC1 proposal (July 2013-June 2017) we got 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 *ACS Pharmacol. & Trans. Sci*. 2029 in collaboration with Drs. Hubbard and Prabha). 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 Drs. Hubbard and Prabha).

In my research group, we have also performed research on the topic of ***ruthenium compounds as anti-cancer agents*** 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, *Chem. A Eur. J.* 2021, *ChemMedChem* 2021 and *Inorg. Chem*. 2021) and on dendrimers

incorporating organometallic ruthenium compounds as anticancer agents (*Dalton Trans* 2016). During my career I have published 72 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 (*ACS Nano* 2019). 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® (*Chem Commun*. 2019, *J. Inorg. Biochem*. 2019, US patent 2021). This project is in collaboration with Memorial Sloan Kettering Cancer Center. These last two projects have been funded by a grant from NIH (SC1) for the period June 2018-June 2022.

More recently, I am the co-founder, director and research area leader of the Brooklyn College Cancer Center for Community Outreach, Research and, Education BCCC-CURE (established in October 2020, (http://bccc.blog.brooklyn.edu/). The mission of the center is to enhance the lives of patients affected by cancer with a special focus on Brooklyn residents. Through this center, Brooklyn College seeks to expand its fundamental (basic and applied) research on cancer and combine research forces with local (New York City) cancer treatment centers and hospitals, and Brooklyn communities, while delivering first-class educational opportunities to our undergraduate and graduate students. I developed the original proposal for the creation of the center and content for the web site, recruited associated directors and other personnel, appointed members of the Advisory Board and raised funds for the operations of the first three years (2020-2022). I have also coordinated scientific seminars and symposia as well as community outreach events, and have worked and assisted on grant submissions for the Center and PIs and on the establishment of partnerships with Cancer Centers and Academic and Research Centers in Brooklyn and NYC area.

Since I joined Brooklyn College in 2006, I have supervised 68 researchers: 7 post-docs, 7 doctoral students (3 already graduated), 3 masters' students (graduated), 41 Bachelors, and 3 high school students. 80% of these researchers are students underrepresented in the physical sciences (minority students, females and persons with disabilities) including MARC and LSAMP students. Many of the undergraduate students were co-authors in publications and 8 of these students joined PhD programs in biomedical areas (MD/PhD chemistry, biochemistry and biology) or sciences (mathematics) while most of the others went to medical schools. I have supervised 6 students from foreign universities who have done either a masters or a PhD research stay in my group and hosted an Assistant Professor (Dr. Jose Cerón-Carrasco) from the Catholic University of Murcia in Spain in summer of 2019. I was the mentor of Prof. Guillermo Gerona-Navarro, an Assistant Professor at the Chemistry Department of Brooklyn College for his SCORE SC2 application (awarded in 2014). He successfully transitioned to a SCORE SC1 award in 2020. I have also mentored Assistant Prof. Mariana Torrente, since August 2015.

I am a regular reviewer for a variety of prestigious journals in chemistry and medicinal chemistry and a regular reviewer of NSF, NIH and PRF grants (including panels) and of some grants from other countries (Canada, Hong Kong, Israel, South Africa, and several European and Latin-American countries) in the areas of medicinal inorganic chemistry, organometallic chemistry and homogeneous catalysis.

B. POSITIONS AND HONORS

Positions and Employment (reverse chronological order)

2020- present	**Director.** Brooklyn College Cancer Center for Community Outreach, Research, and Education BCCC-CURE, Brooklyn College, CUNY.
2018 Spring- present	**Faculty, Biochemistry PhD Program**, The Graduate Center, CUNY.
July 2017-June 2020	**Chairperson**. Chemistry Department, Brooklyn College, CUNY.
August 2016-present	**Professor**. Chemistry Department, Brooklyn College, 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.

October 2006- present	**Faculty, Chemistry PhD Program**, The Graduate Center, CUNY.
2006-2010	**Assistant Professor (Inorganic Chemistry).** Chemistry Department, Brooklyn College, CUNY.
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.
2002-2006	**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.
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.
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.

Honors and Awards (reverse chronological order)

2021-2022	Jaques Edward Levy Professor (Brooklyn College).
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.
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.
2002-2006	Ramon y Cajal Senior Research Position. Most prestigious Spanish Research Fellowship for Young Investigators.

C. CONTRIBUTION TO SCIENCE

72 peer reviewed articles (including 2 reviews, 3 book chapters, and a book review), 3 US patents issued, over eighty-five communications or invited talks at National and International Conferences. Five articles in preparation for submission in 2022.

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_2Ag and Au_2Cu Complexes with Mesityl Bridging Ligands. X-Ray Structure of the One-dimensional Chain Polymer [{Au(μ-mes)($AsPh_3$}$_2$Ag]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_6Ag 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}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 $[AuPPh_3]^+$ fragments to act as Li^+ or $MgBr^-$ equivalents (based on the isolobality of $AuPPh_3^+$ and H^+ and Li^+). In this way I was able to use R-Au-PPh_3 compounds as transmetallating agents to different metallic centers (Au^{III}, Pt^{II}, Pd^{II}, Ni^{II}, Fe^{III}, and Ti^{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-$C_6H_4PPh_2$ 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 and copper complexes in homogenous catalysis (including water-soluble and fluorous recyclable catalysts).** (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 in gold catalysis (6 as PI or co-PI). At the time I started the project in 2003 there were only 5 publications 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 340 citations). In terms of recyclable catalysts (gold and copper) I published 6 papers, and 2 book chapters all as PI or co-PI. I worked in: 1) the preparation of recyclable fluorous 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. I select two publications below.

- ´Organometallic Gold(III) Compunds 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) **Metallodrugs as antimicrobial and anticancer agents**. **Targeted delivery vehicles for anticancer metal-based drugs.** I have worked in this field at Brooklyn College since 2009 funded by NIH (NIGMS SC2 grant 2010-2013, NCI S1 grant 2013-2017, and 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. In addition, one 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 36 papers on this topic and a chapter of book since 2009, and I have three patents issued. I have also published 5 papers in the area of antimicrobial metallodrugs. I have been invited to talk at different International Conferences (including keynote lectures at the 18th International Conference on Biological Inorganic Chemistry, ICBIC 18" Brazil, 2017: International Symposium on Bioorganometallic Chemistry (ISBOMC) 2021 and 7th Latin American meeting on Biological Inorganic Chemistry (LABIC) 2021). I was the organizer and co-Chair of the '1st International Symposium on Clinical and Experimental Metallodrugs in Medicine: Cancer Chemotherapy' held in Honolulu (December 12th-15th, 2015, http://cemm.brooklyn.cuny.edu/) and partly funded by a R13 grant (Contel, PI). I was discussion leader in the session of "Recent Developments in Metallodrugs" (Gordon Conference on Metals in Medicine, June 2018) and will be invited speaker and power hour organizer and discussion leader at the Gordon Conference on Metals in Medicine, June 2022. Some 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.; Pechenyy, Y.; Layek, B.; Prabha, S.; **Contel**, **M**. *Cancer Med*. **2019**, *8*, 4304.
-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.
- 'Auranofin-Based Analogues Are Effective Against Clear Cell Renal Carcinoma in vivo and Display no Significant Systemic Toxicity'. Elie, B.T.; Hubbard, K.; Layek, B.; Yang, W.S.; Prabha, S.; Ramos, J.W.; **Contel, M**. *ACS Pharmacol. Trans. Sci*. **2020**. *3(4)*, 644.

The list of published work in my bibliography: (unfinished):
https://www.ncbi.nlm.nih.gov/myncbi/1tGxfI5TFD6kc/bibliography/public/

D. RESEARCH SUPPORT (LAST THREE YEARS)

Ongoing Research support

NIH/NIGMS 2SC1GM127278-05A1 Contel (PI) 06/01/18-05/31/2022
Biodegradable nanocarriers and antibodies as targeting delivery vehicles for cancer metallodrugs
Goal: "To develop safe and highly selective metal-based anticancer chemotherapeutics by either incorporation into biodegradable enzyme-specific cleavable nanocarriers or by conjugation to specific monoclonal antibodies". The PI oversees the synthetic procedures, characterization, biological data collection and analysis, interactions with collaborators, and writing of manuscripts.

Completed Research Support (Last three years)

NIH/NCI 1SC1CA182844-03 Contel (PI) 07/01/13-05/31/2018
Titanium-gold-based chemotherapeutics for prostate and kidney cancer
Goal: "To develop heterometallic titanium-gold anticancer chemotherapeutics for the treatment of renal and prostate cancers". The PI oversees the synthetic procedures, characterization, biological data collection and analysis, interactions with collaborators, and writing of manuscripts.