BIOGRAPHICAL SKETCH
NAME: Gevaert, Olivier

eRA COMMONS USER NAME (credential, e.g., agency login): GEVAERT.OLIVIER

POSITION TITLE: Assistant Professor in Medicine (Biomedical Informatics)

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 College, KAHO, Ghent Belgium	B.S.	06/2001	Industrial Engineering
University College, KAHO, Ghent Belgium	M.S.	06/2003	Industrial Engineering
University of Leuven, KUL, Belgium	M.S.	06/2004	Artificial Intelligence
University of Leuven, KUL, Belgium	Ph.D.	12/2008	Bioinformatics
University of Leuven, KUL, Belgium	Postdoctoral	12/2009	Bioinformatics
Stanford University, California	Postdoctoral	11/2012	Bioinformatics

A. Personal Statement

I'm an Assistant Professor of Medicine (Biomedical informatics) at the Stanford University School of Medicine. The Gevaert lab long-term focus is on multi-scale data fusio**n**: the development of machine learning methods for biomedical decision support using multi-scale biomedical data. Radiomics, radiogenomics and imaging genomics are instantiations of this long-term research theme and the Gevaert lab has a track record in this field. We led key contributions in the field of imaging genomics/radiogenomics involving work in lung cancer (**Radiology** 2012, **Radiology** 2017), brain tumors (**Radiology** 2014, **Science Translational Medicine** 2015), colorectal cancer (**Radiotherapy & Oncology** 2017) and hepatocellular carcinoma (**JMI** 2017). Our work in imaging genomics is focused on developing a framework for non-invasive precision medicine.

Next, my background is in bioinformatics. Previously I pioneered data fusion work using Bayesian and kernel methods studying transcriptomics of breast and ovarian cancer. My subsequent work concerned the development of methods for multi-omics data fusion. This resulted in the development of MethylMix, to identify differentially methylated genes, and AMARETTO, a computational method to integrate DNA methylation, copy number and gene expression data to identify cancer modules with publications in methodological journals such as **Bioinformatics**, **Genome Biology** and molecular/clinical journals such as **Cancer Research, Nature Medicine, Cell, Cancer Cell, Cell Reports** and **Cell Stem Cell**. Additionally, my lab focuses on linking molecular data with cellular and tissue-level phenotypes. In summary, my lab has an interdisciplinary focus on developing novel algorithms for multi-scale biomedical data fusion.

B. Positions and Honors

Professional Experience

2013- Assistant Professor, Stanford University

Other Experience and Professional Memberships

2006- Member, International Society for Computational Biology (ISCB)
2010- Member, American Association for Cancer Research (AACR)
2013- Member, Society of Neuro-Oncology (SNO)
2014- Member, American Society of Neuro-radiology (ASNR)
2015- Member, American Medical Informatics Association (AMIA)

Honors and Awards

2004-2008	Ph.D. grant of the agency for Innovation by Science and Technology in Flanders
2009-2010	Honorary Fulbright Scholar of the Commission for Educational Exchange between the United States of America, Belgium and Luxembourg
2009-2010	Henri Benedictus Fellow of the King Baudouin Foundation
2009-2010	Fellow of the Belgian American Educational Foundation (BAEF)
2009-2012	Post-doctoral researcher of the Fund for scientific research Flanders
2014	Invited speaker, American Society for Neuro Radiology
2013/14/15/17	Invited speaker, Radiological Society of North America (RSNA)

C. Contributions to Science

1. Multi-scale modeling, imaging genomics/radiogenomics, radiomics.

Imaging genomics is a growing field and application area in multi-scale data fusion whereby macroscopic phenotypes from medical imaging are linked with molecular phenotypes. I published initial **radiogenomics** work applied on lung cancer patients (Gevaert et al. Radiology 2012, Zhou et al. Radiology 2017, Gevaert et al. Sci. Reports 2017) and more recently in glioblastoma (Itakura et al. Science Translational Medicine 2015), colorectal cancer and hepatocellular carcinoma. In an editorial accompanying our results our work was described as "[this work] offers an original approach to exploring the clinical prognostic value of imaging-genomics. This approach cleverly leverages both private and public data in a complementary way and advances the field by offering a promising new avenue for early exploratory imaging research that desires to study conventional clinical imaging relationships with cellular genomics." More recently, we identified **three imaging based subtypes** for adult brain tumors and linked them to activation of canonical pathways implicating drug treatment (Itakura et al. Science Translational Medicine 2015). This contribution was featured in **Lancet Oncology,** among others**,** as a key innovation by flipping the paradigm of subtyping disease by using imaging instead of molecular data first.

a. **Gevaert O**, Echegaray S, Khuong A, Hoang CD, Shrager JB, Jensen KC, Berry GJ, Guo HH, Lau C, Plevritis SK, Rubin DL, Napel S, Leung AN. Predictive radiogenomics modeling of EGFR mutation status in lung cancer. *Scientific Reports* 2017 Jan 31;7:41674. doi: 10.1038/srep41674. PubMed PMID: 28139704; PubMed Central PMCID: PMC5282551.
b. Zhou M, Leung A, Echegaray S, Gentles A, Shrager JB, Jensen KC, Berry GJ, Plevritis SK, Rubin D, Napel S, **Gevaert O**. Radiogenomics mapping of non-small cell lung cancer identifies prognostic relationships between semantic image features and metagenes captured using RNA sequencing. *Radiology*, 2017 Jul 20:161845. doi: 10.1148/radiol.2017161845.
c. Itakura H, Achrol A, Mitchell AL, Loya JJ, Liu T, Westbroek EM, Feroze AH, Rodriguez S, Echegaray S, Azad TD, Yeom KW, Napel S, Rubin DL, Chang SD, Harsh GR IV, **Gevaert O**. Magnetic resonance image features identify glioblastoma phenotypic subtypes with distinct molecular pathway activities. *Science Translational Medicine*, 2015 Sep 2;7(303):303ra138. PMID: 26333934; PubMed Central PMCID: PMC4666025.
d. **Gevaert O**, Xu J, Hoang C, Leung A, Xu Y, Quon A, Rubin D, Napel S, and Plevritis S: Non-small cell lung cancer: identifying prognostic imaging biomarkers by leveraging public gene expression microarray data--methods and preliminary results. *Radiology*, 264:387-96, 2012. PMID: 22723499, PMC3401348.

2. Computational biology and bioinformatics

Initially I developed an extensive framework using Bayesian algorithms (Gevaert et al. Bioinformatics 2016). Next, we included algorithms using support vector machines and kernel methods. More recently, we have developed **CoINcIDE** a method to identify subtypes across many gene expression cohorts (Planey et al. Genome Medicine 2016). Next, I have expanded our work into regularized regression approaches to build data fusion methods for multi-omics data. We developed a novel algorithm called **MethylMix** to identify differentially methylated genes that are also transcriptionally predictive. We also show that our methylation based clustering identified unique disease clusters not identified by gene expression, copy number or mutation data. MethylMix is available for the community as an R package (Gevaert Bioinformatics 2015). We contributed bioinformatics expertise to a large multi-institutional transcriptomic study of **intestinal stem cells** and showed two transcriptomic subtypes (Yan et al. Cell Stem Cell 2017).

a. Planey RK, **Gevaert O**. CoINcIDE: A framework for discovery of patient subtypes across multiple datasets. *Genome Medicine* 2016 Mar 9;8(1):27. doi:10.1186/s13073-016-0281-4. PubMed PMID: 26961683; PubMed Central PMCID: PMC4784276.
b. Cedoz PL, Prunello M, Brennan K, **Gevaert O**. MethylMix 2.0: an R package for identifying DNA methylation genes. Bioinformatics 2018, In Press.
c. Yan KS, **Gevaert O**, Probert CS, Zheng GXY, Larkin KA, Davies PS, Cheng Z, Kaddis JS, Wilhelmy J, Grimes S, Han A, Roelf K, Corney D, Terry JM, Belgrader P, Mikkelsen TS, Wang F, von Furstenberg RJ, Chrissy M, Cartwright CA, Niland JC, Hong Y, Carrington J, Breault D, Epstein J, Houchen CW, Lynch JP, Martin MG, Curtis CM, Ji HP, Li L. Henning SJ, Wong MH, Kuo CJ. Mature enteroendocrine cells possess injury-inducible reserve stem cell function. *Cell Stem Cell*, 2017 Jul 6;21(1):78-90.e6. doi: 10.1016/j.stem.2017.06.014.
d. **Gevaert O**., De Smet F., Timmerman D., Moreau Y., and De Moor B. Predicting the prognosis of breast cancer by integrating clinical and microarray data with Bayesian networks, Bioinformatics, 22(14):e184–190, 2006

3. Diagnostic subtyping and prognostics signatures for cancer

We have developed prognostic signature for several cancers. More specifically, we have described a seven-gene signature for predicting prognosis of **hepatocellular carcinoma** (van Malenstein et al. Clinical Cancer Research, 2010) and we have developed a prognostic signature for **thyroid cancer**, a disease that suffers from overtreatment (Brennan et al. BMC Cancer 2016). Our signature can be used to select patients for less intensive treatment to avoid unnecessary comorbidity. Next, we have described novel subtypes for head and neck squamous carcinoma based on DNA methylation, and discovered two novel subtypes: the CIMP atypical/idiopathic subtype (Brennan et al. Sci. Rep 2017) and the NSD1 subtype (Brennan et al. EBioMedicine 2017).

a. Brennan K, Shin JH, Tay JT, Prunello M, Gentles AJ, Sunwoo JB, **Gevaert O**. NSD1 inactivation defines an immune cold, DNA hypomethylated subtype in squamous cell carcinoma, Scientific Reports, 2017 Dec 6;7(1):17064. doi: 10.1038/s41598-017-17298-x.
b. Brennan K, Koenig JL, Gentles AJ, Sunwoo JB, **Gevaert O**. Identification of an atypical etiological head and neck squamous carcinoma subtype featuring the CpG island methylator phenotype. EBioMedicine. 2017 Mar;17:223-236. doi:10.1016/j.ebiom.2017.02.025. Epub 2017 Mar 1. PubMed PMID: 28314692; PubMed Central PMCID: PMC5360591.
c. Brennan K, Holsinger C, Dosiou C, Sunwoo JB, Akatsu H, Haile R, **Gevaert O**. Development of prognostic signatures for intermediate-risk papillary thyroid cancer. BMC Cancer. 2016 Sep 15;16(1):736. doi: 10.1186/s12885-016-2771-6. PubMed PMID: 27633254; PubMed Central PMCID: PMC5025616.
d. van Malenstein H., **Gevaert O.**, Libbrecht L., Daemen A., Allemeersch J., Nevens F., Van Hummelen P,, Cassiman D., De Moor B., Verslype C. and van Pelt J. A 7 Gene Set Associated with Chronic Hypoxia of Prognostic Importance in Hepatocellular Carcinoma, Clinical Cancer Research, 2010, Aug 15, 16(16),4278-88

4. Cancer bioinformatics

We developed novel computational algorithms to model cancer omics data and identify novel oncogenes and tumor suppressor genes, to define subtypes and to develop multivariate models for prognosis or therapy response. We contributed to a large study on adult glioma's and defined **7 novel glioma molecular subtypes** based on molecular data that correlate better with survival than histology (Gravendeel et al. Cancer research 2009). We correctly predicted the target of microRNA miR-483 as PDLIM2, validated in colon organoids (Li et al. Nature Medicine 2014), and we studied multi-drug resistance in ovarian cancer (Dubey et al. Cancer Research 2016).

a. Dubey R, Lebensohn A, Bahrami-Nejad Z, Marceau C, Champion M, **Gevaert O**, Sikic BI, Carette JE, Rohatgi R. Chromatin-remodeling complex SWI/SNF controls multidrug resistance by transcriptionally regulating the drug efflux pump ABCB1. Cancer Res. 2016 Aug 8. pii: canres.0716.2016.
b. Li X., Nadauld L., Ootani A., Corney D., Pai R., **Gevaert O.,** Cantrell M., Rack P., Neal JT., Chan C., Yeung T., Yuan X., Wilhelmy J., Robine S., Attardi L., Plevritis S.K., Hung K., Chen C., Ji H., Kuo C. Oncogenic transformation of diverse gastrointestinal tissues in primary organoid culture. *Nature Medicine*, 2014, Jul;20(7):769-77. PMID: 24859528; PMCID: PMC4087144

c. Gravendeel L, Kouwenhoven M, **Gevaert O**, de Rooi J, Stubbs A, Duijm J, Daemen A, Bleeker F, Bralten L, Kloosterhof N, De Moor B, van der Spek P, Kros J, Sillevis Smitt P, and van den Bent M: French P. Intrinsic gene expression profiles of gliomas are a better predictor of survival than histology. *Cancer Res*, 69:9065-72, 2009. PMID: 19920198.

5. Pancancer modeling

I developed multiple frameworks for pancancer modeling using biomedical data fusion. We developed bioinformatic algorithms **MethylMix**, **AMARETTO and CaMoDi**, these are algorithms for multi-omics data fusion (Manolakos et al. BMC Genomics 2014). They model gene expression, DNA copy number and DNA methylation data and represent this as cancer modules, and have been shown to outperform existing methods. We applied MethylMix on over 4000 cancer cases across twelve cancer sites and identified pancancer hyper and hypomethylated genes, novel subgroups and pancancer methylation patterns. These results showed for the first time a pancancer differential methylation analysis by combining over 4000 cases across twelve cancer sites in a pancancer map. This map shows novel methylation patterns across twelve cancer sites and we identified four mixed pancancer clusters (Gevaert et al. Genome Biology 2015). Similarly, we have developed a pancancer analysis using AMARETTO and identify two novel genes: GPX2 a cancer driver gene in smoking related cancers and OAS2 marking an anti-viral pancancer subtype (Champion et al. EBioMedicine 2017). More recently we are linking multi-omics data across scales with cellular and imaging phenotypes and extend towards multi-scale biomedical data fusion.

a. Liu Y, Sethi N, Hinoue T, Schneider B, Cherniack AD, Sanchze-Vega F, Seoane JA, Fashidfar F, Bowlby R, Islam M, Kim J, Chatila W, Akbani R, Kanchi RS, Rabkin CS, Willis JE, Wang KK, McCall SJ, Mishra L, Ojesina AI, Bullman S, Sekhar C, Lazar A, **The Cancer Genome Atlas Research Network**, Thorsson V, Bass AJ, Laird PW. Comparative molecular analysis of gastrointestinal adenocarcinomas. Cancer Cell 2018, In Press.
b. Campbell JD*, Yau C*, Bowlby R*, Liu Y*, Brennan K*, Fan H, Taylor A, Wang C, Walter V, Akbani R, Averett B, Creighton CJ, Coarfa C, Shih J, Cherniack AD, **Gevaert O**, Shen H, ANur P, Chen J, Cheng H, Hayes N, Bullman S, Pedamallu S, Ojesina A, Sadeghi S, Mungall K, Benz C, Schultz A, Kanchi R, Gay CM, Hegde A, Diao L, Wang J, Sumazin P, Gunaratne P, Donehower L, Rader JS, Zuna R, Al-Ahmadie H, Lazar A, Drill E, Shen R, Won C, The Cancer Genome Atlas Network, Stuart JM, Larid PW, Hoadley K, Weinstein J, Peto M, Pickering CR, Chen Z, Van Waes C. Genomic, pathway network and immunologic features distinguishing squamous carcinomas. Cell Reports 2018, In Press.
c. Malta M, Sokolov A, Gentles AJ, Burzykowski T, Poisson L, Weinstein JN, Kaminska B, Huelsken J, Larsson O, **Gevaert O**, Colaprico A, Czerwinska P, Mauzrek S, Mishra L, Heyn H, Krasnitz A, Godwin A, Lazar A, The Cancer Genome Atlas Research Network, Stuart JM, Hoadley KA, Laird PW, Noushmehr H, Wiznerowicz M. Comprehensive analysis of cancer stemness. Cell. 2018, In Press.
d. Champion M, Brennan K, Croonenborghs T, Gentles AJ, Pochet N, **Gevaert O**. Module analysis captures pancancer genetic and epigenetic deregulated cancer driver genes for smoking and antiviral response. EBioMedicine 2018 Jan;27:156-166. doi: 10.1016/j.ebiom.2017.11.028. Epub 2017 Dec 1.

Complete List of Published Work in My NCBI:
http://www.ncbi.nlm.nih.gov/myncbi/collections/bibliography/47665038/

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

R01 EB020527 (Gevaert) 2/15/15 – 1/31/19
NIH/NIBIB Role: PI
Radiogenomics Framework for Non-invasive Personalized Medicine
The major goal of this project is to capture quantitatively the 3D morphology of tumors on medical images and apply frameworks that identify cancer driver genes from genomic and transcriptomic data.

U01 DE025188 (Kuo/Sunwoo/Gevaert) 7/1/15 – 6/30/19
NIH/NCI Role: MPI
Identification of Cooperative Genetic Alterations in the Pathogenesis of Oral Cancer
The major goals of this project are to use bioinformatics algorithms to integrate genomic data in Oral Squamous Cell Carcinoma TCGA data sets to identify master regulators of biologic processes.

U01 CA217875 (Kuo) 8/1/17 – 7/31/22
NIH/NCI Role: Co-investigator
Organoid-Based Discovery of Oncogenic Drivers and Treatment Resistance Mechanisms
The major goal of this proposal is to use bioinformatics strategies to identify novel cancer targets that will subsequently be modeled in organoid cultures of mouse and human tissues.
Role: Co-Investigator

U01 CA187947 (Napel/Rubin) 7/1/15 – 6/30/20
NIH/NCI Role: Co-investigator
Computing, Optimizing and Evaluating Quantitative Cancer Imaging Biomarkers
The major goal of this project is to develop a cloud-based resource for generating image features of tumors and evaluating their absolute and relative efficacy for predicting dependent variables, such as response, survival, and cancer genomics.

Completed Research Support

R01 CA160251 (Napel/Plevritis) 9/1/11 – 7/31/17
NIH/NCI Role: Co-investigator
Tools for Linking and Mining Image and Genomic Data in Non-Small Cell Lung Cancer
The major goal of this project is to develop tools for creating an integrated database of imaging, clinical, and genomic features in non-small cell lung cancer and to mine it for relationships to prognosis.

U01 CA176299 (Kuo/Ji) 5/2/13 – 4/30/17
NIH/NCI Role: Co-investigator
Functional Analysis of Oncogenic Networks and Drug Response in Primary Organoids
The major goal of this project is to use novel statistical methods to pre-filter the enormous amount of mutational data from human cancers and directly validate these mutations as relevant to cancer in "organoid" cultures.

U01 DK085527 (Kuo) 9/22/09 – 8/31/19 (inactive)
NIH/NIDDK Role: Co-investigator
Regulation of Actively Proliferating and Quiescent Intestinal Stem Cells
The major goal of this project is to identify and molecularly characterize intestinal stem cells by identifying processes that control proliferation and differentiation of quiescent stem cells.
Role: Co-Investigator