
Année de publication : 2019

Judith Abécassis, Anne-Sophie Hamy, Cécile Laurent, Benjamin Sadacca, Hélène Bonsang-Kitzis, Fabien Reyat, Jean-Philippe Vert (2019 Nov 8)

Assessing reliability of intra-tumor heterogeneity estimates from single sample whole exome sequencing data.

PloS one : e0224143 : [DOI : 10.1371/journal.pone.0224143](https://doi.org/10.1371/journal.pone.0224143)

Résumé

Tumors are made of evolving and heterogeneous populations of cells which arise from successive appearance and expansion of subclonal populations, following acquisition of mutations conferring them a selective advantage. Those subclonal populations can be sensitive or resistant to different treatments, and provide information about tumor aetiology and future evolution. Hence, it is important to be able to assess the level of heterogeneity of tumors with high reliability for clinical applications. In the past few years, a large number of methods have been proposed to estimate intra-tumor heterogeneity from whole exome sequencing (WES) data, but the accuracy and robustness of these methods on real data remains elusive. Here we systematically apply and compare 6 computational methods to estimate tumor heterogeneity on 1,697 WES samples from the cancer genome atlas (TCGA) covering 3 cancer types (breast invasive carcinoma, bladder urothelial carcinoma, and head and neck squamous cell carcinoma), and two distinct input mutation sets. We observe significant differences between the estimates produced by different methods, and identify several likely confounding factors in heterogeneity assessment for the different methods. We further show that the prognostic value of tumor heterogeneity for survival prediction is limited in those datasets, and find no evidence that it improves over prognosis based on other clinical variables. In conclusion, heterogeneity inference from WES data on a single sample, and its use in cancer prognosis, should be considered with caution. Other approaches to assess intra-tumoral heterogeneity such as those based on multiple samples may be preferable for clinical applications.

Année de publication : 2016

Laura Sabiani, Gilles Houvenaeghel, Mellie Heinemann, Fabien Reyat, Jean Marc Classe, Monique Cohen, Jean Rémy Garbay, Sylvia Giard, Hélène Charitansky, Nicolas Chopin, Roman Rouzier, Emile Daraï, Charles Coutant, Pierre Azuar, Pierre Gimbergues, Richard Villet, Christine Tunon de Lara, Eric Lambaudie (2016 Aug 2)

Breast cancer in young women: Pathologic features and molecular phenotype.

Breast (Edinburgh, Scotland) : 109-116 : [DOI : S0960-9776\(16\)30116-3](https://doi.org/10.1186/s12874-016-0301-3)

Résumé

Controversy exists about the prognosis of breast cancer in young women. Our objective was to describe clinicopathological and prognostic features to improve adjuvant treatment indications.

Rana Hatem, Rania El Botty, Sophie Chateau-Joubert, Jean-Luc Servely, Dalila Labiod, Ludmilla de Plater, Franck Assayag, Florence Coussy, Céline Callens, Sophie Vacher, Fabien Reyat, Sabina Cosulich, Véronique Diéras, Ivan Bièche, Elisabetta Marangoni (2016 Jul 5)

Targeting mTOR pathway inhibits tumor growth in different molecular subtypes of triple-negative breast cancers.

Oncotarget : [DOI : 10.18632/oncotarget.10195](https://doi.org/10.18632/oncotarget.10195)

Résumé

Triple-negative breast cancers (TNBC) are characterized by frequent alterations in the PI3K/AKT/mTOR signaling pathway. In this study, we analyzed PI3K pathway activation in 67 patient-derived xenografts (PDX) of breast cancer and investigated the anti-tumor activity of the mTOR inhibitor everolimus in 15 TNBC PDX with different expression and mutational status of PI3K pathway markers. Expression of the tumor suppressors PTEN and INPP4B was lost in 55% and 76% of TNBC PDX, respectively, while mutations in PIK3CA and AKT1 genes were rare. In 7 PDX treatment with everolimus resulted in a tumor growth inhibition higher than 50%, while 8 models were classified as low responder or resistant. Basal-like, LAR (Luminal AR), mesenchymal and HER2-enriched tumors were present in both responder and resistant groups, suggesting that tumor response to everolimus is not restricted to a specific TNBC subtype. Analysis of treated tumors showed a correlation between tumor response and post-treatment phosphorylation of AKT, increased in responder PDX, while PI3K pathway markers at baseline were not sufficient to predict everolimus response. In conclusion, targeting mTOR decreased tumor growth in 7 out of 15 TNBC PDX tested. Response to everolimus occurred in different TNBC subtypes and was associated with post-treatment increase of P-AKT.

Marick Laé, Philippe La Rosa, Jonas Mandel, Fabien Reyat, Philippe Hupé, Philippe Terrier, Jérôme Couturier (2016 May 22)

Whole-genome profiling helps to classify phyllodes tumours of the breast.

Journal of clinical pathology : [DOI : jclinpath-2016-203684](https://doi.org/10.1136/jclinpath-2016-203684)

Résumé

The aim of this study was to analyse a series of borderline and malignant phyllodes tumours (PTs) of the breast by whole-genome profiling to identify genomic markers that could help to recognise potentially malignant tumours within borderline tumours.

Enora Laas, Peter Mallon, Francois P Duhoux, Amina Hamidouche, Roman Rouzier, Fabien Reyat (2016 Feb 20)

Low Concordance between Gene Expression Signatures in ER Positive HER2 Negative Breast Carcinoma Could Impair Their Clinical Application.

PloS one : e0148957 : [DOI : 10.1371/journal.pone.0148957](https://doi.org/10.1371/journal.pone.0148957)

Résumé

Numerous prognostic gene expression signatures have been recently described. Among the signatures there is variation in the constituent genes that are utilized. We aim to evaluate prognostic concordance among eight gene expression signatures, on a large dataset of ER positive HER2 negative breast cancers.

Claire Sénéchal, Fabien Reyat, Nasrine Callet, Pascale This, Catherine Noguès, Dominique Stoppa-Lyonnet, Emmanuelle Fourme (2016 Feb 8)

[Hormonotherapy for breast cancer prevention: What about women with genetic predisposition to breast cancer?].

Bulletin du cancer : 273-81 : [DOI : 10.1016/j.bulcan.2016.01.001](https://doi.org/10.1016/j.bulcan.2016.01.001)

Résumé

In France, women carrying BRCA1/2 mutation, at an identified high risk of breast cancer are recommended to undergo breast MRI screening. That screening does not however prevent the risk of developing a breast cancer. The only alternative to breast cancer screening available in France is surgical prevention by prophylactic mastectomy. An interesting option for women who wish to reduce their breast cancer risk, but are unready for prophylactic mastectomy is a preventive hormonal treatment by aromatase inhibitors, or selective estrogens receptor modulators (SERMs). Reliable clinical trials show the efficiency of tamoxifen, raloxifen, exemestane, and anastrozole especially, in reducing breast cancer incidence by 33%, 34%, 65% and 53% respectively. This article tries to sum up the main published trials of breast cancer prevention with hormonal treatment, and presents the latest American and English clinical guidelines concerning hormonal prevention for women at high risk of breast cancer, and starts thinking about the possibilities of hormonoprevention, especially among women carrying a BRCA1/2 mutation in France.

Année de publication : 2015

Hélène Bonsang-Kitzis, Léonor Chaltier, Lisa Belin, Alexia Savignoni, Roman Rouzier, Marie-Paule Sablin, Florence Lerebours, François-Clément Bidard, Paul Cottu, Xavier Sastre-Garau, Marick Laé, Jean-Yves Pierga, Fabien Reyat (2015 Dec 20)

Beyond Axillary Lymph Node Metastasis, BMI and Menopausal Status Are Prognostic Determinants for Triple-Negative Breast Cancer Treated by Neoadjuvant Chemotherapy.

PloS one : e0144359 : [DOI : 10.1371/journal.pone.0144359](https://doi.org/10.1371/journal.pone.0144359)

Résumé

Triple-negative breast cancers (TNBC) are a specific subtype of breast cancers with a particularly poor prognosis. However, it is a very heterogeneous subgroup in terms of clinical

behavior and sensitivity to systemic treatments. Thus, the identification of risk factors specifically associated with those tumors still represents a major challenge. A therapeutic strategy increasingly used for TNBC patients is neoadjuvant chemotherapy (NAC). Only a subset of patients achieves a pathologic complete response (pCR) after NAC and have a better outcome than patients with residual disease.

Anne-Sophie Hamy-Petit, Lisa Belin, Hélène Bonsang-Kitzis, Caroline Paquet, Jean-Yves Pierga, Florence Lerebours, Paul Cottu, Roman Rouzier, Alexia Savignoni, Marick Lae, Fabien Reyat (2015 Dec 15)

Pathological complete response and prognosis after neoadjuvant chemotherapy for HER2-positive breast cancers before and after trastuzumab era: results from a real-life cohort.

British journal of cancer : 44-52 : [DOI : 10.1038/bjc.2015.426](https://doi.org/10.1038/bjc.2015.426)

Résumé

Trastuzumab was introduced a decade ago and has improved outcomes for HER2-positive breast cancer. We investigated the factors predictive of pathological complete response (pCR), prognostic factors for disease-free survival (DFS), and interactions between pCR and DFS after neoadjuvant treatment.

Matahi Moarii, Valentina Boeva, Jean-Philippe Vert, Fabien Reyat (2015 Oct 30)

Changes in correlation between promoter methylation and gene expression in cancer.

BMC genomics : 873 : [DOI : 10.1186/s12864-015-1994-2](https://doi.org/10.1186/s12864-015-1994-2)

Résumé

Methylation of high-density CpG regions known as CpG Islands (CGIs) has been widely described as a mechanism associated with gene expression regulation. Aberrant promoter methylation is considered a hallmark of cancer involved in silencing of tumor suppressor genes and activation of oncogenes. However, recent studies have also challenged the simple model of gene expression control by promoter methylation in cancer, and the precise mechanism of and role played by changes in DNA methylation in carcinogenesis remains elusive.

Matahi Moarii, Fabien Reyat, Jean-Philippe Vert (2015 Oct 15)

Integrative DNA methylation and gene expression analysis to assess the universality of the CpG island methylator phenotype.

Human genomics : 26 : [DOI : 10.1186/s40246-015-0048-9](https://doi.org/10.1186/s40246-015-0048-9)

Résumé

The CpG island methylator phenotype (CIMP) was first characterized in colorectal cancer but since has been extensively studied in several other tumor types such as breast, bladder, lung, and gastric. CIMP is of clinical importance as it has been reported to be associated with prognosis or response to treatment. However, the identification of a universal molecular basis to define CIMP across tumors has remained elusive.

Lea Rossi, Denise Stevens, Jean-Yves Pierga, Florence Lerebours, Fabien Rey, Mathieu Robain, Bernard Asselain, Roman Rouzier (2015 Jul 28)

Impact of Adjuvant Chemotherapy on Breast Cancer Survival: A Real-World Population.

PloS one : e0132853 : [DOI : 10.1371/journal.pone.0132853](https://doi.org/10.1371/journal.pone.0132853)

Résumé

The impact of adjuvant chemotherapy on breast cancer prognosis has been demonstrated in randomized trials, but its impact is unknown in real-world populations. The aim of this study was to evaluate the effect of adjuvant chemotherapy on the survival of breast cancer patients in an unselected population.

Vincent Gardeux, Rachid Chelouah, Maria F Barbosa Wanderley, Patrick Siarry, Antônio P Braga, Fabien Rey, Roman Rouzier, Lajos Pusztai, René Natowicz (2015 May 19)

Computing molecular signatures as optima of a bi-objective function: method and application to prediction in oncogenomics.

Cancer informatics : 33-45 : [DOI : 10.4137/CIN.S21111](https://doi.org/10.4137/CIN.S21111)

Résumé

Filter feature selection methods compute molecular signatures by selecting subsets of genes in the ranking of a valuation function. The motivations of the valuation functions choice are almost always clearly stated, but those for selecting the genes according to their ranking are hardly ever explicit.

Caroline Malhaire, Delphine Hequet, Marie-Christine Falcou, Jean-Guillaume Feron, Anne Tardivon, Alexandre Leduey, Eugénie Guillot, Véronique Mosseri, Roman Rouzier, Benoit Couturaud, Fabien Rey (2015 Apr 28)

Outcome of oncoplastic breast-conserving surgery following bracketing wire localization for large breast cancer.

Breast (Edinburgh, Scotland) : 370-5 : [DOI : 10.1016/j.breast.2015.02.037](https://doi.org/10.1016/j.breast.2015.02.037)

Résumé

The purpose of this study was to evaluate the outcome of breast conserving surgery comparing oncoplastic surgery (OS) and standard lumpectomy (SL) after preoperative bracketing wire localization of large neoplastic lesions.

Moarii M., Reyat F., Vert J.P. (2015 Jan 1)

Integrative DNA methylation and gene expression analysis to assess the universality of the CpG island methylator phenotype

Human genomics : 9 : 1

Résumé

Année de publication : 2014

Peter Mallon, François Ganachaud, Caroline Malhaire, Raphael Brunel, Brigitte Sigal-Zafrani, Jean-Guillaume Feron, Benoit Couturaud, Alfred Fitoussi, Fabien Reyat (2014 Oct 8)

Bilateral poly implant prothèse implant rupture: an uncommon presentation.

Plastic and reconstructive surgery. Global open : e29 : [DOI : 10.1097/GOX.0b013e318298e026](https://doi.org/10.1097/GOX.0b013e318298e026)

Résumé

A woman in her 50s underwent delayed bilateral Poly Implant Prothèse implant reconstruction following mastectomy for breast cancer. Symptoms of implant rupture developed 43 months after surgery with an erythematous rash on her trunk. The rash then spread to her reconstructed breast mounds. Initial ultrasound scan and magnetic resonance imaging were normal; however, subsequent magnetic resonance imaging demonstrated left implant rupture only. In theater, following removal of both implants, both were found to be ruptured. The rash on her trunk resolved within 3 weeks in the postoperative period. Chemical analyses of silicone in both implants confirmed a nonauthorized silicone source; in addition, the chemical structure was significantly different between the left and right implant, perhaps explaining the variation in presentation.