

Hétérogénéité Génétique des Cancer du sein

Pr. X Pivot
CHRU Besançon

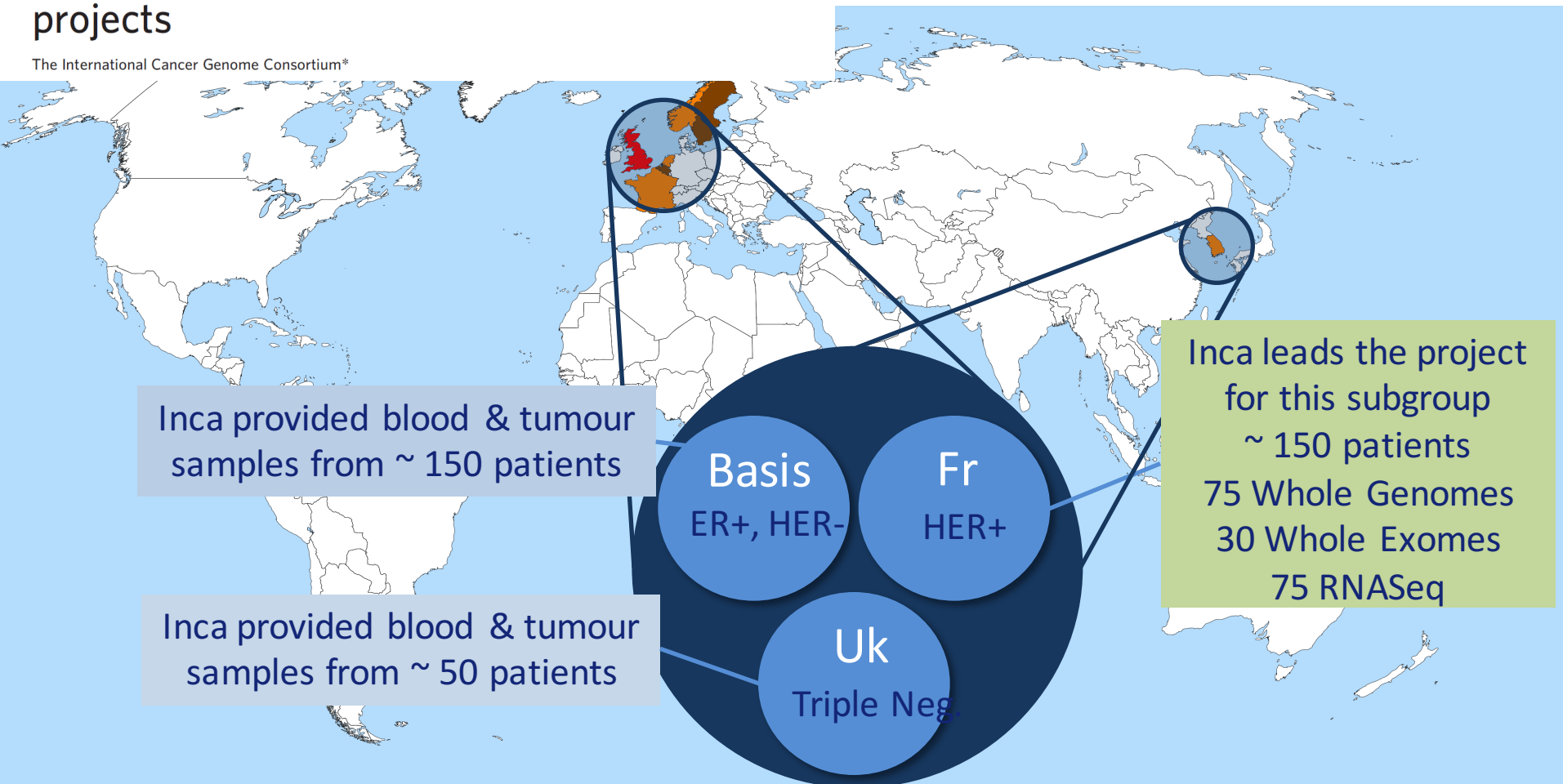
PERSPECTIVES



International
Cancer Genome
Consortium

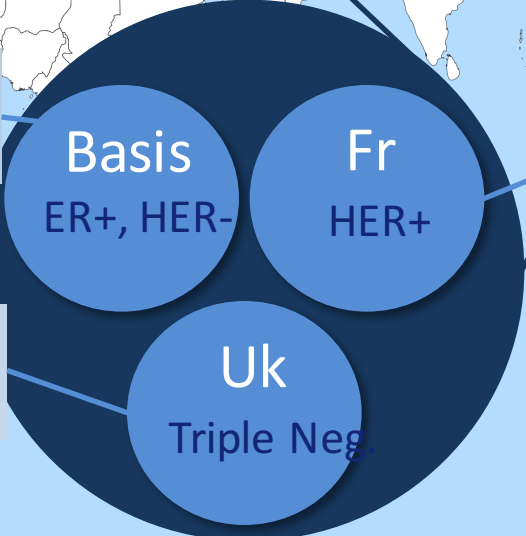
International network of cancer genome projects

The International Cancer Genome Consortium*



Inca provided blood & tumour samples from ~ 150 patients

Inca provided blood & tumour samples from ~ 50 patients



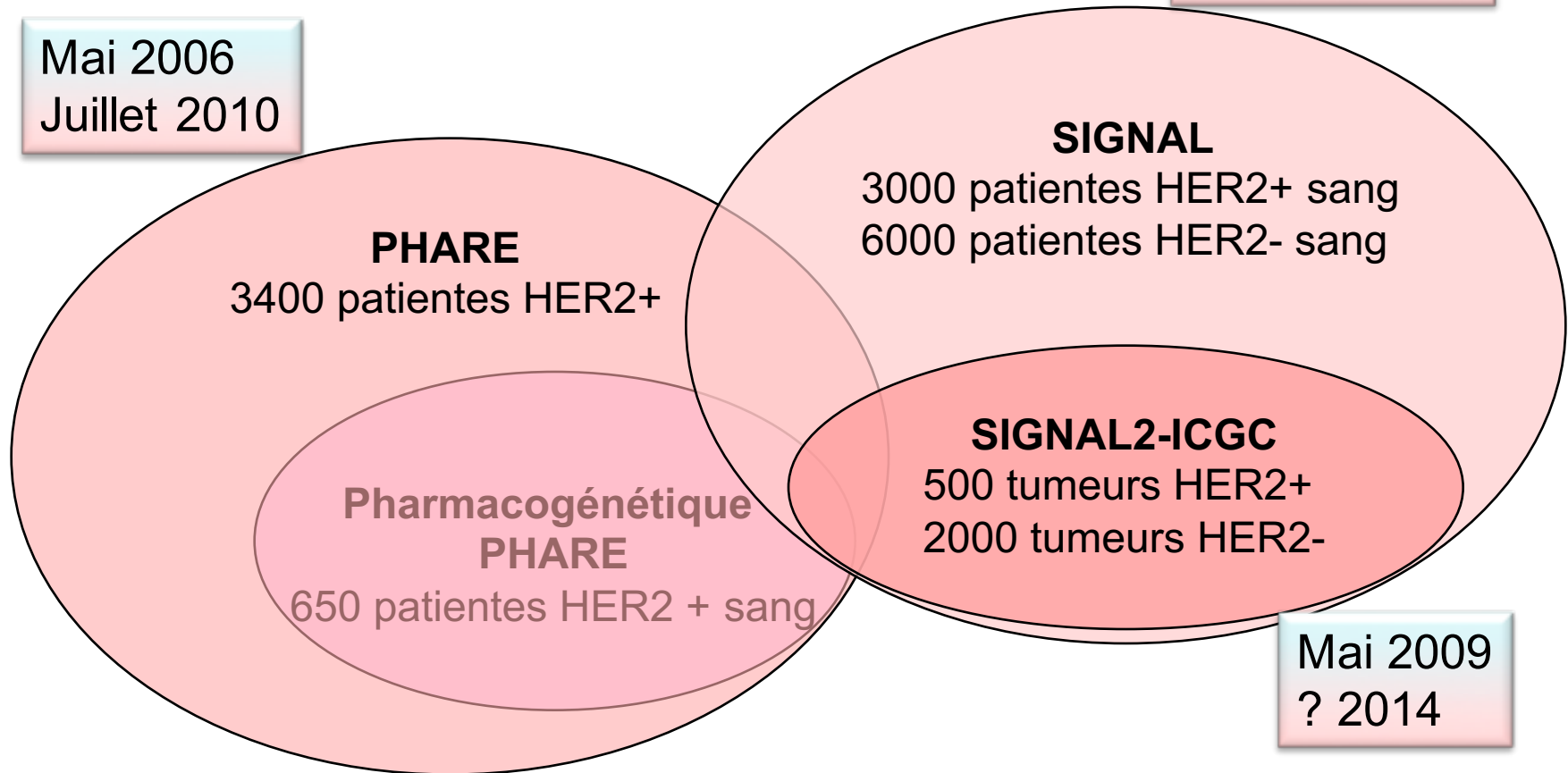
Inca leads the project for this subgroup
~ 150 patients
75 Whole Genomes
30 Whole Exomes
75 RNASeq

Total sequenced & analyzed
560 tumours
(~140 from INCa)

Études sein INCa

Mai 2009
Octobre 2011

Mai 2006
Juillet 2010



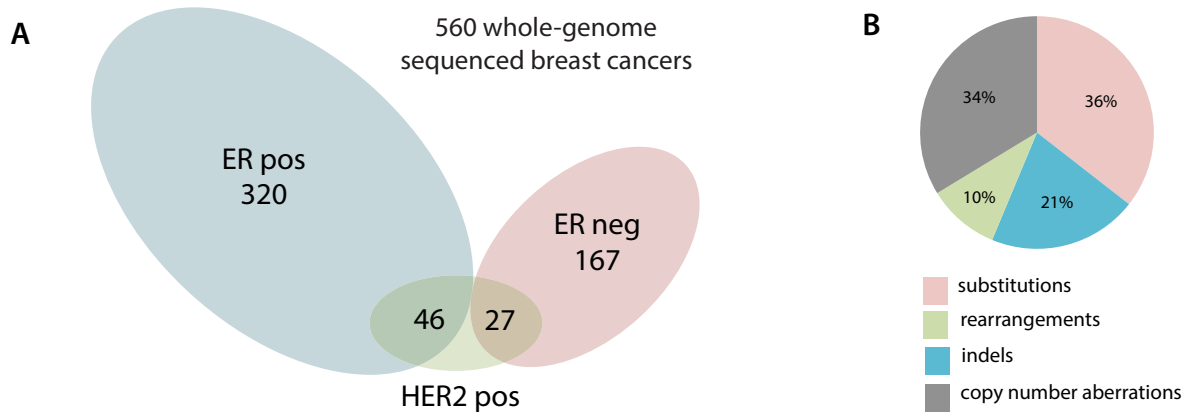
Mai 2009
? 2014

- Suivi clinique pour 5 ans
- Echantillon de sang (optionnel)

- Suivi clinique pour 5 ans
- Questionnaire épidémiologique SIGNAL
- Echantillon de sang +
- Tumeur pour SIGNAL2-ICGC-BASIS

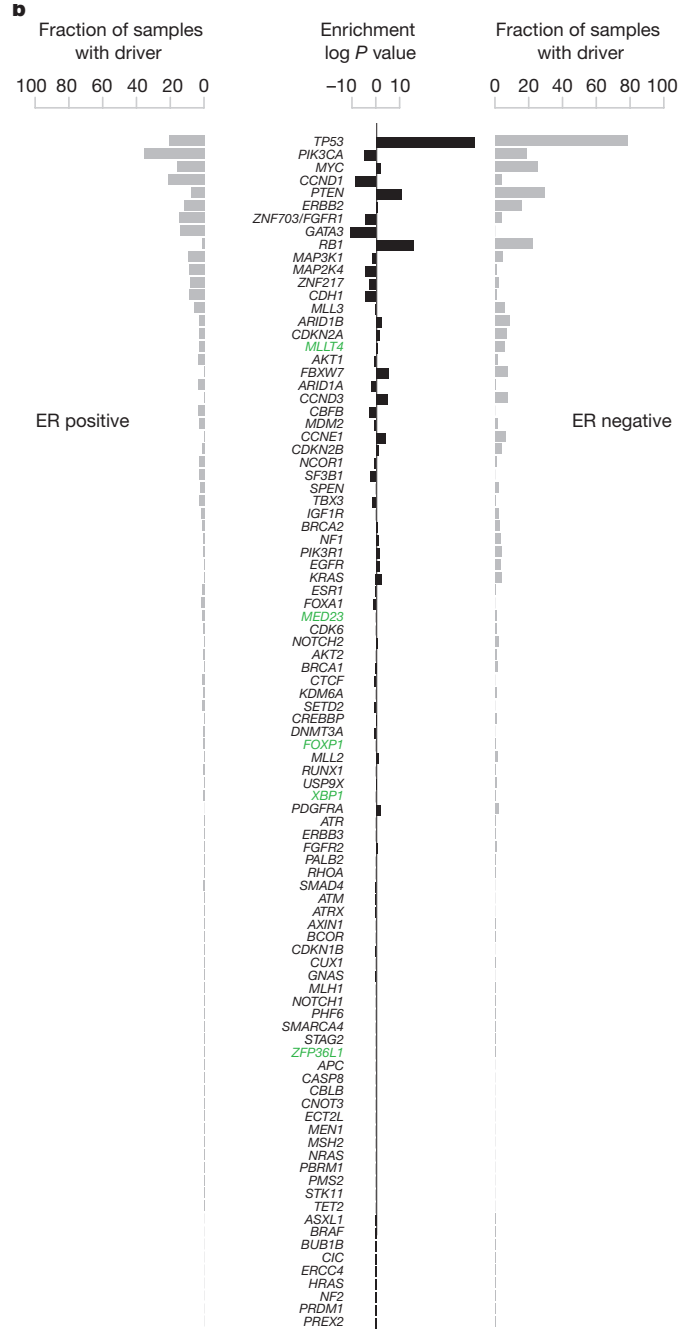
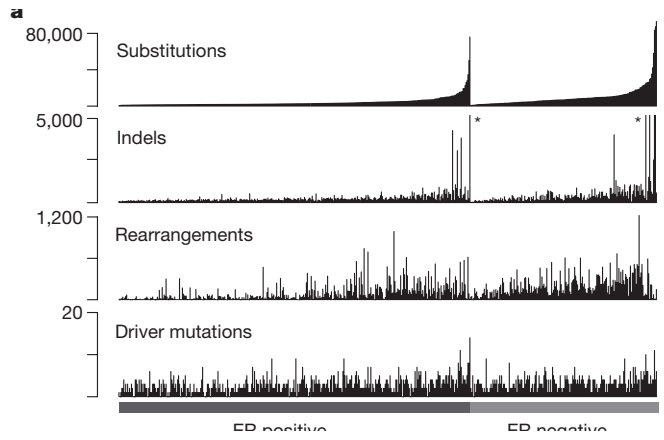
Landscape of somatic mutations in 560 breast cancer whole-genome sequences

Serena Nik-Zainal^{1,2}, Helen Davies¹, Johan Staaf³, Manasa Ramakrishna¹, Dominik Glodzik¹, Xueqing Zou¹, Inigo Martincorena¹, Ludmil B. Alexandrov^{1,4,5}, Sancha Martin¹, David C. Wedge¹, Peter Van Loo^{1,6}, Young Seok Ju¹, Marcel Smid⁷, Arie B. Brinkman⁸, Sandro Morganello⁹, Miriam R. Aure^{10,11}, Ole Christian Lingjærde^{11,12}, Anita Langerød^{10,11}, Markus Ringnér³, Sung-Min Ahn¹³, Sandrine Boyault¹⁴, Jane E. Brock¹⁵, Annegien Broeks¹⁶, Adam Butler¹, Christine Desmedt¹⁷, Luc Dirix¹⁸, Serge Dronov¹, Aquila Fatima¹⁹, John A. Foekens⁷, Moritz Gerstung¹, Gerrit K. J. Hooijer²⁰, Se Jin Jang²¹, David R. Jones¹, Hyung-Yong Kim²², Tari A. King²³, Savitri Krishnamurthy²⁴, Hee Jin Lee²¹, Jeong-Yeon Lee²⁵, Yilong Li¹, Stuart McLaren¹, Andrew Menzies¹, Ville Mustonen¹, Sarah O'Meara¹, Iris Pauporté²⁶, Xavier Pivrot²⁷, Colin A. Purdie²⁸, Keiran Raine¹, Kamna Ramakrishnan¹, F. Germán Rodríguez-González⁷, Gilles Romieu²⁹, Anieta M. Sieuwerts⁷, Peter T. Simpson³⁰, Rebecca Shepherd¹, Lucy Stebbings¹, Olafur A. Stefansson³¹, Jon Teague¹, Stefania Tommasi³², Isabelle Treilleux³³, Gert G. Van den Eynden^{18,34}, Peter Vermeulen^{18,34}, Anne Vincent-Salomon³⁵, Lucy Yates¹, Carlos Caldas³⁶, Laura van't Veer¹⁶, Andrew Tutt^{37,38}, Stian Knappskog^{39,40}, Benita Kiat Tee Tan^{41,42}, Jos Jonkers¹⁶, Åke Borg³, Naoto T. Ueno²⁴, Christos Sotiriou¹⁷, Alain Viari^{43,44}, P. Andrew Futreal^{1,45}, Peter J. Campbell¹, Paul N. Span⁴⁶, Steven Van Laere¹⁸, Sunil R. Lakhani^{30,47}, Jorunn E. Eyfjord³¹, Alastair M. Thompson^{28,48}, Ewan Birney⁹, Hendrik G. Stunnenberg⁸, Marc J. van de Vijver²⁰, John W. M. Martens⁷, Anne-Lise Børresen-Dale^{10,11}, Andrea L. Richardson^{15,19}, Gu Kong²², Gilles Thomas⁴⁴ & Michael R. Stratton¹



Landscape of somatic mutations in 560 breast cancer whole-genome sequences

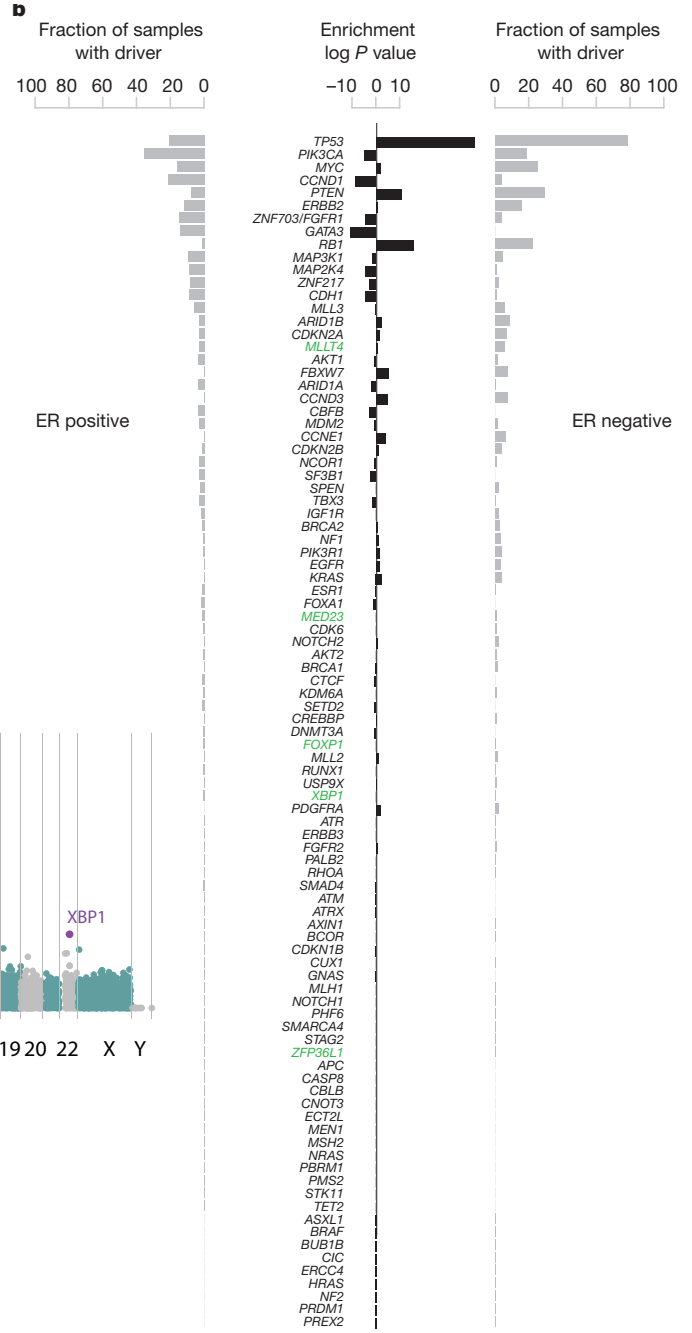
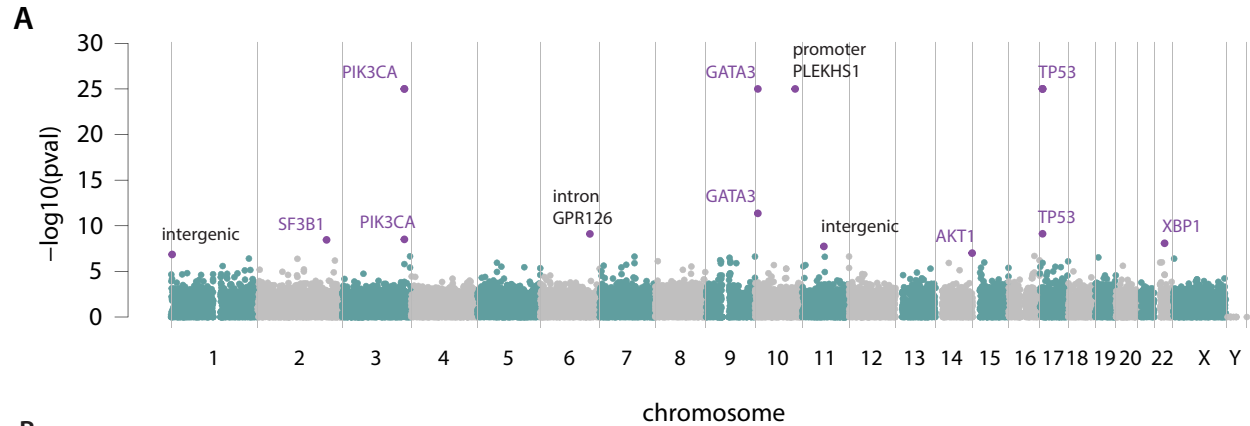
Serena Nik-Zainal^{1,2}, Helen Davies¹, Johan Staaf³, Manasa Ramakrishna¹, Dominik Glodzik¹, Xueqing Zou¹, Inigo Martincorena¹, Ludmil B. Alexandrov^{1,4,5}, Sancha Martin¹, David C. Wedge¹, Peter Van Loo^{1,6}, Young Seok Ju¹, Marcel Smid⁷, Arie B. Brinkman⁸, Sandro Morganello⁹, Miriam R. Aure^{10,11}, Ole Christian Lingjærde^{11,12}, Anita Langerød^{10,11}, Markus Ringnér³, Sung-Min Ahn¹³, Sandrine Boyault¹⁴, Jane E. Brock¹⁵, Annegien Broeks¹⁶, Adam Butler¹, Christine Desmedt¹⁷, Luc Dirix¹⁸, Serge Dronov¹, Aquila Fatima¹⁹, John A. Foekens⁷, Moritz Gerstung¹, Gerrit K. J. Hooijer²⁰, Se Jin Jang²¹, David R. Jones¹, Hyung-Yong Kim²², Tari A. King²³, Savitri Krishnamurthy²⁴, Hee Jin Lee²¹, Jeong-Yeon Lee²⁵, Yilong Li¹, Stuart McLaren¹, Andrew Menzies¹, Ville Mustonen¹, Sarah O'Meara¹, Iris Pauport²⁶, Xavier Pivot²⁷, Colin A. Purdie²⁸, Keiran Raine¹, Kamna Ramakrishnan¹, F. Germán Rodríguez-González⁷, Gilles Romieu²⁹, Anieta M. Sieuwerts⁷, Peter T. Simpson³⁰, Rebecca Shepherd¹, Lucy Stebbings¹, Olafur A. Stefansson³¹, Jon Teague¹, Stefania Tommasi³², Isabelle Treilleux³³, Gert G. Van den Eynden^{18,34}, Peter Vermeulen^{18,34}, Anne Vincent-Salomon³⁵, Lucy Yates¹, Carlos Caldas³⁶, Laura van't Veer¹⁶, Andrew Tutt^{37,38}, Stan Knappekog^{39,40}, Benita Kiat Tee Tan^{41,42}, Jos Jonkers¹⁶, Åke Borg³, Naoto T. Ueno²⁴, Christos Sotiriou¹⁷, Alain Viari^{43,44}, P. Andrew Futreal^{1,45}, Peter J. Campbell¹, Paul N. Span⁴⁶, Steven Van Laere¹⁸, Sunil R. Lakhani^{30,47}, Jorunn E. Eyfjord³¹, Alastair M. Thompson^{28,48}, Ewan Birney⁹, Hendrik G. Stunnenberg⁵, Marc J. van de Vijver²⁰, John W. M. Martens⁷, Anne-Lise Borresen-Dale^{10,11}, Andrea L. Richardson^{15,19}, Gu Kong²², Gilles Thomas⁴⁴ & Michael R. Stratton¹



- TP53
- PIK3CA
- MYC
- CCND1
- PTEN
- ERBB2
- ZNF703/FGFR1
- GATA3
- RB1
- MAP3K1
- MAP2K4
- ZNF217
- CDH1
- MLL3
- AFR1B
- CDKN2A
- MLL2
- AKT1
- FBXW7
- AFR1A
- CCND3
- CBFB
- MDM2
- CCNE1
- CDKN2B
- NCOR1
- SF3B1
- SPEN
- TBX3
- IGF1R
- BRC A2
- NF1
- PIK3R1
- EGFR
- KRAS
- ESR1
- FOXA1
- MED23
- CDK6
- NOTO2
- AKT2
- BRC A1
- CTCF
- KDM6A
- SETD2
- CREBBP
- DNMT3A
- FOXP1
- MLL2
- RUNX1
- USP9X
- XBP1
- PDGFRA
- ATR
- ERBB3
- FGFR2
- PALB2
- RHOA
- SMAD4
- ATM
- ATRX
- AXIN1
- BCOR
- CDKN1B
- CUX1
- GNAS
- MLH1
- NOTCH1
- PHF6
- SMARCA4
- STAG2
- ZFP36L1
- APC
- CASP8
- CBLB
- CNOT3
- ECT2L
- MEN1
- MSH2
- NRAS
- PBRM1
- PMS2
- STK11
- TET2
- ASXL1
- BRAF
- BUB1B
- CIC
- ERCC4
- HRAS
- NF2
- PRDM1
- PREX2

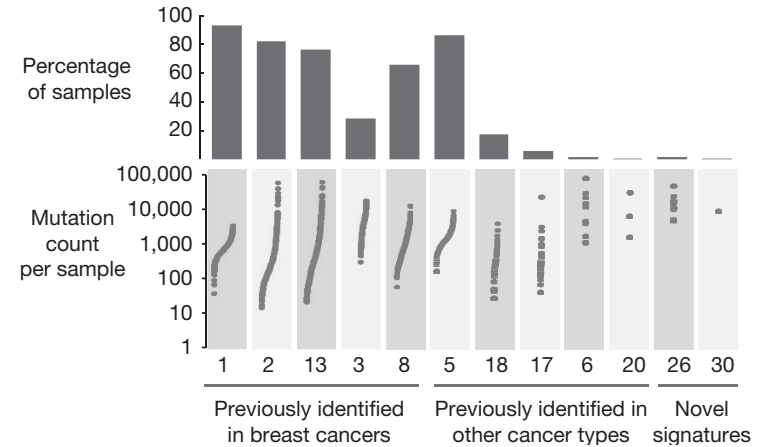
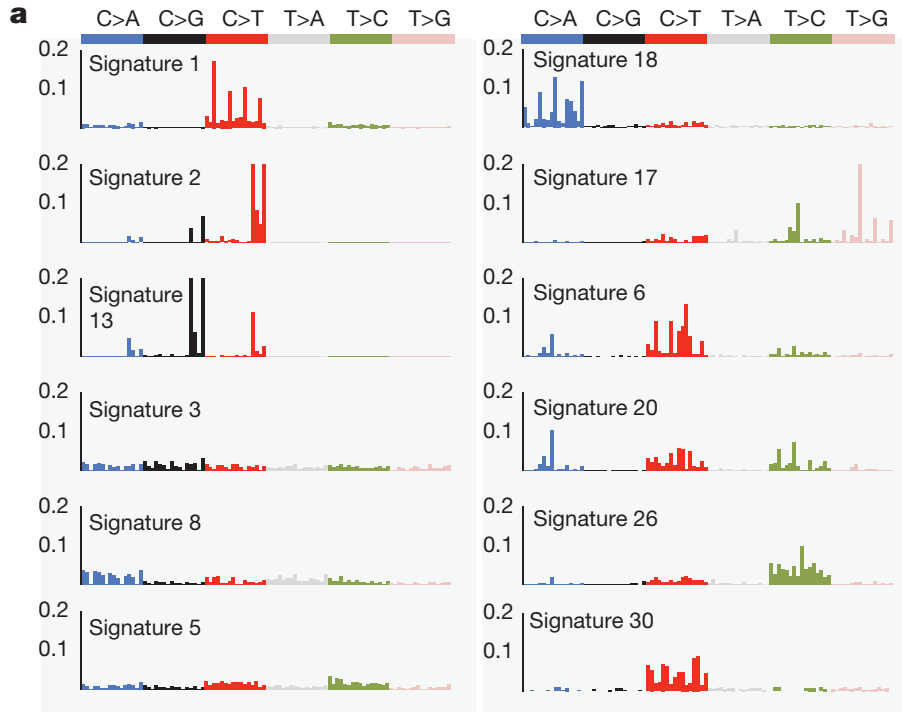
Landscape of somatic mutations in 560 breast cancer whole-genome sequences

Serena Nik-Zainal^{1,2}, Helen Davies¹, Johan Staaf³, Manasa Ramakrishna¹, Dominik Glodzik¹, Xueqing Zou¹, Inigo Martincorena¹, Ludmil B. Alexandrov^{1,4,5}, Sancha Martin¹, David C. Wedge¹, Peter Van Loo^{1,6}, Young Seok Ju¹, Marcel Smid⁷, Arie B. Brinkman⁸, Sandro Morgnani⁹, Miriam R. Aure^{10,11}, Ole Christian Lingjærde^{11,12}, Anita Langerød^{10,11}, Markus Ringnér³, Sung-Min Ahn¹³, Sandrine Boyault¹⁴, Jane E. Brock¹⁵, Annegien Broeks¹⁶, Adam Butler¹, Christine Desmedt¹⁷, Luc Dirix¹⁸, Serge Dronov¹, Aquila Fatima¹⁹, John A. Foekens¹, Moritz Gerstung¹, Gerrit K. J. Hooijer²⁰, Se Jin Jang²¹, David R. Jones¹, Hyung-Yong Kim²², Tari A. King²³, Savitri Krishnamurthy²⁴, Hee Jin Lee²¹, Jeong-Yeon Lee²⁵, Yilong Li¹, Stuart McLaren¹, Andrew Menzies¹, Ville Mustonen¹, Sarah O'Meara¹, Iris Pauport²⁶, Xavier Pivot²⁷, Colin A. Purdie²⁸, Keiran Raine¹, Kamna Ramakrishnan¹, F. Germán Rodríguez-González⁷, Gilles Romieu²⁹, Anieta M. Sieuwerts⁷, Peter T. Simpson³⁰, Rebecca Shepherd¹, Lucy Stebbings¹, Olafur A. Stefansson³¹, Jon Teague¹, Stefania Tommasi³², Isabelle Treilleux³³, Gert G. Van den Eynden^{18,34}, Peter Vermeulen^{18,34}, Anne Vincent-Salomon³⁵, Lucy Yates¹, Carlos Caldas³⁶, Laura van't Veer¹⁶, Andrew Tutt^{37,38}, Stian Knappskog^{39,40}, Benita Kiat Tee Tan^{41,42}, Jos Jonkers¹⁶, Åke Borg³, Naoto T. Ueno²⁴, Christos Sotiropoulos¹⁷, Alain Viari^{43,44}, P. Andrew Futreal^{1,45}, Peter J. Campbell¹, Paul N. Span⁴⁶, Steven Van Laere¹⁸, Sunil R. Lakhani^{30,47}, Jorunn E. Eyfjord³¹, Alastair M. Thompson^{28,48}, Ewan Birney⁹, Hendrik G. Stunnenberg⁵, Marc J. van de Vijver²⁰, John W. M. Martens⁷, Anne-Lise Borresen-Dale^{10,11}, Andrea L. Richardson^{15,19}, Gu Kong²², Gilles Thomas⁴⁴ & Michael R. Stratton¹



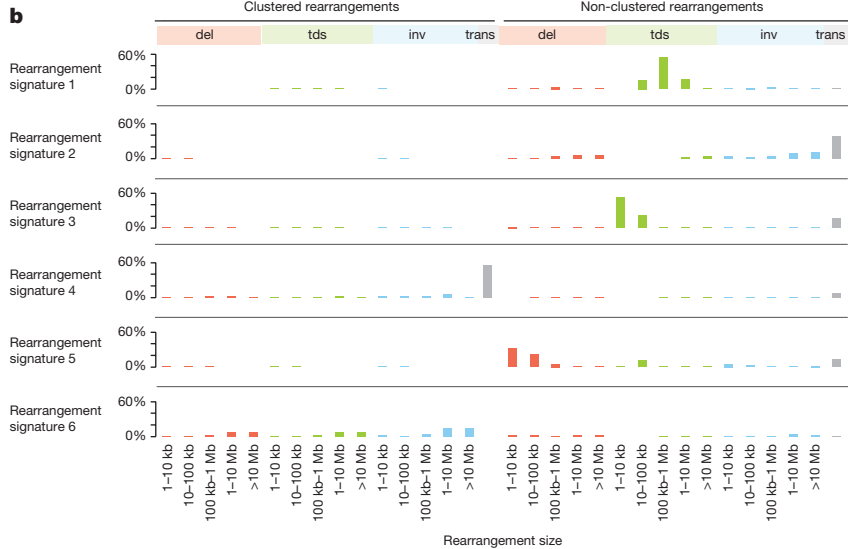
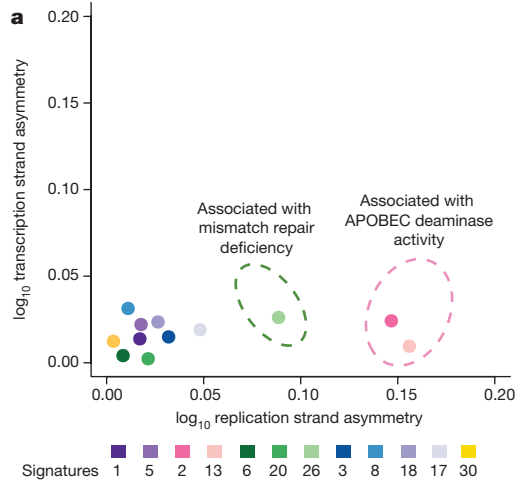
Landscape of somatic mutations in 560 breast cancer whole-genome sequences

Serena Nik-Zainal^{1,2}, Helen Davies¹, Johan Staaf³, Manasa Ramakrishna¹, Dominik Glodzik¹, Xueqing Zou¹, Inigo Martincorena¹, Ludmil B. Alexandrov^{1,4,5}, Sancha Martin¹, David C. Wedge¹, Peter Van Loo^{1,6}, Young Seok Ju¹, Marcel Smid⁷, Arie B. Brinkman⁸, Sandro Morgantella⁹, Miriam R. Aure^{10,11}, Ole Christian Lingjærde^{11,12}, Anita Langerød^{10,11}, Markus Ringnér³, Sung-Min Ahn¹³, Sandrine Boyault¹⁴, Jane E. Brock¹⁵, Annegien Broeks¹⁶, Adam Butler¹, Christine Desmet¹⁷, Luc Dirix¹⁸, Serge Dronov¹, Aquila Fatima¹⁹, John A. Foekens¹⁵, Moritz Gerstung¹, Gerrit K. J. Hooijer²⁰, Se Jin Jang²¹, David R. Jones¹, Hyung-Yong Kim²², Tari A. King²³, Savitri Krishnamurthy²⁴, Hee Jin Lee²¹, Jeong-Yeon Lee²⁵, Yilong Li¹, Stuart McLaren¹, Andrew Menzies¹, Ville Mustonen¹, Sarah O'Meara¹, Iris Pauporté²⁶, Xavier Pivot²⁷, Colin A. Purdie²⁸, Keiran Raine¹, Kamna Ramakrishnan¹, F. Germán Rodríguez-González⁷, Gilles Romieu²⁹, Anieta M. Sieuwerts⁷, Peter T. Simpson³⁰, Rebecca Shepherd¹, Lucy Stebbings¹, Olafur A. Stefansson³¹, Jon Teague¹, Stefania Tommasi³², Isabelle Treilleux³³, Gert G. Van den Eynden^{18,34}, Peter Vermeulen^{18,34}, Anne Vincent-Salomon³⁵, Lucy Yates¹, Carlos Caldas³⁶, Laura van't Veer¹⁶, Andrew Tutt^{37,38}, Stian Knappskog^{39,40}, Benita Kiat Tee Tan^{41,42}, Jos Jonkers¹⁶, Åke Borg³, Naoto T. Ueno²⁴, Christos Sotiriou¹⁷, Alain Viari^{43,44}, P. Andrew Futreal^{1,45}, Peter J. Campbell¹, Paul N. Span⁴⁶, Steven Van Laere¹⁸, Sunil R. Lakhani^{30,47}, Jorunn E. Eyfjord³¹, Alastair M. Thompson^{28,48}, Ewan Birney⁹, Hendrik G. Stunnenberg⁵, Marc J. van de Vijver²⁰, John W. M. Martens⁷, Anne-Lise Borresen-Dale^{10,11}, Andrea L. Richardson^{15,19}, Gu Kong²², Gilles Thomas⁴⁴ & Michael R. Stratton¹



Landscape of somatic mutations in 560 breast cancer whole-genome sequences

Serena Nik-Zainal^{1,2}, Helen Davies¹, Johan Staaf³, Manasa Ramakrishna¹, Dominik Glodzik¹, Xueqing Zou¹, Inigo Martincorena¹, Ludmil B. Alexandrov^{1,4,5}, Sancha Martin¹, David C. Wedge¹, Peter Van Loo^{1,6}, Young Seok Ju¹, Marcel Smid⁷, Arie B. Brinkman⁸, Sandro Morganello⁹, Miriam R. Aure^{10,11}, Ole Christian Lingjærde^{11,12}, Anita Langerød^{10,11}, Markus Ringnér³, Sung-Min Ahn¹³, Sandrine Boyault¹⁴, Jane E. Brock¹⁵, Annegien Broeks¹⁶, Adam Butler¹, Christine Desmedt¹⁷, Luc Dirix¹⁸, Serge Dronov¹, Aquila Fatima¹⁹, John A. Foekens¹, Moritz Gerstung¹, Gerrit K. J. Hooijer²⁰, Se Jin Jang²¹, David R. Jones¹, Hyung-Yong Kim²², Tari A. King²³, Savitri Krishnamurthy²⁴, Hee Jin Lee²¹, Jeong-Yeon Lee²⁵, Yilong Li¹, Stuart McLaren¹, Andrew Menzies¹, Ville Mustonen¹, Sarah O'Meara¹, Iris Pauporté²⁶, Xavier Pivot²⁷, Colin A. Purdie²⁸, Keiran Raine¹, Kamna Ramakrishnan¹, F. Germán Rodríguez-González¹, Gilles Romieu²⁹, Anieta M. Sieuwerts⁷, Peter T. Simpson³⁰, Rebecca Shepherd¹, Lucy Stebbings¹, Olafur A. Stefansson³¹, Jon Teague¹, Stefania Tommasi³², Isabelle Treilleux³³, Gert G. Van den Eynden^{18,34}, Peter Vermeulen^{18,34}, Anne Vincent-Salomon³⁵, Lucy Yates¹, Carlos Caldas³⁶, Laura van't Veer¹⁶, Andrew Tutt^{37,38}, Stian Knappskog^{39,40}, Benita Kiat Tee Tan^{41,42}, Jos Jonkers¹⁶, Åke Borg³, Naoto T. Ueno²⁴, Christos Sotiropoulos¹⁷, Alain Viari^{43,44}, P. Andrew Futreal^{1,45}, Peter J. Campbell¹, Paul N. Span⁴⁶, Steven Van Laere¹⁸, Sunil R. Lakhani^{30,47}, Jorunn E. Eyfjord³¹, Alastair M. Thompson^{28,48}, Ewan Birney⁹, Hendrik G. Stunnenberg⁵, Marc J. van de Vijver²⁰, John W. M. Martens⁷, Anne-Lise Borresen-Dale^{10,11}, Andrea L. Richardson^{15,19}, Gu Kong²², Gilles Thomas⁴⁴ & Michael R. Stratton¹



ARTICLE

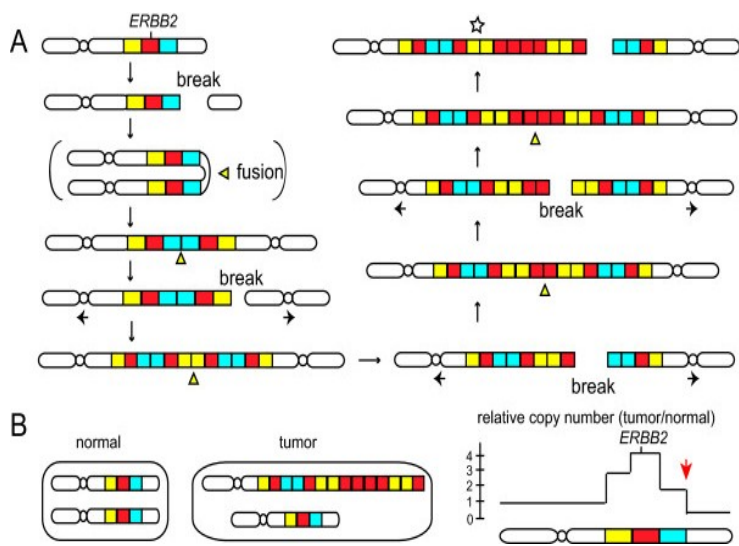
Received 3 Dec 2015 | Accepted 12 Jun 2016 | Published 13 Jul 2016

DOI: 10.1038/ncomms12222 OPEN

A whole-genome sequence and transcriptome perspective on HER2-positive breast cancers

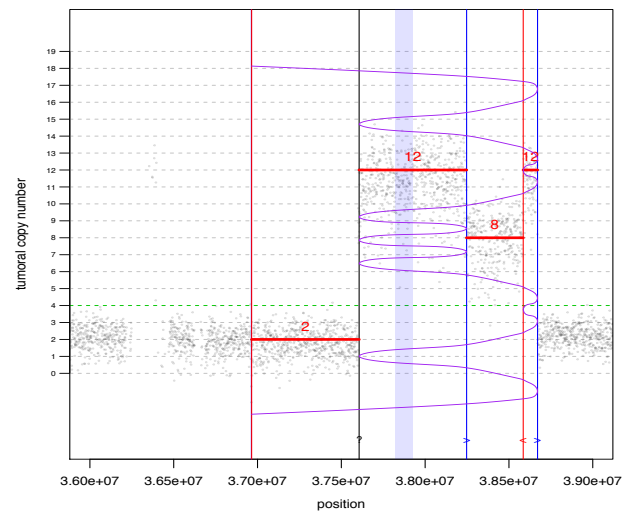
Anthony Ferrari¹, Anne Vincent-Salomon², Xavier Pivot³, Anne-Sophie Sertier¹, Emilie Thomas¹, Laurie Tonon¹, Sandrine Boyault⁴, Eskeatnaf Mulugeta⁵, Isabelle Treilleux⁶, Gaëtan MacGrogan⁷, Laurent Arnould⁸, Janice Kielbassa¹, Vincent Le Texier¹, Héléne Blanche⁹, Jean-François Deleuze⁹, Jocelyne Jacquemier¹⁰, Marie-Christine Mathieu¹¹, Frédérique Penault-Llorca¹², Frédéric Bibeau¹³, Odette Mariani¹⁴, Cécile Mannina¹⁵, Jean-Yves Pierga¹⁶, Olivier Trédan¹⁷, Thomas Bachelot¹⁷, Hervé Bonnefoi¹⁸, Gilles Romieu¹⁹, Pierre Fumoleau⁸, Suzette Delaloge¹¹, Maria Rios²⁰, Jean-Marc Ferrer²¹, Carole Tarpin²², Catherine Boutelle²³, Fabien Calvo²⁴, Ivo Glynne Gu^{25,26}, Marta Gu^{25,26}, Sancha Martin²⁷, Serena Nik-Zainal^{27,28}, Michael R. Stratton²⁷, Iris Pauporté²⁹, Pierre Saintigny^{30,31,32}, Daniel Birnbaum³³, Alain Vian^{1,34} & Gilles Thomas¹

Breakage-Fusion-Bridge

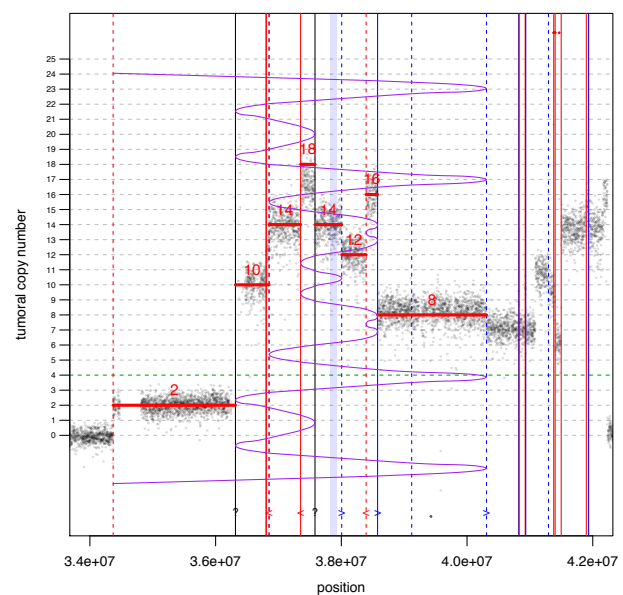


from Marotta et al. Breast Cancer Research 2012

PI078



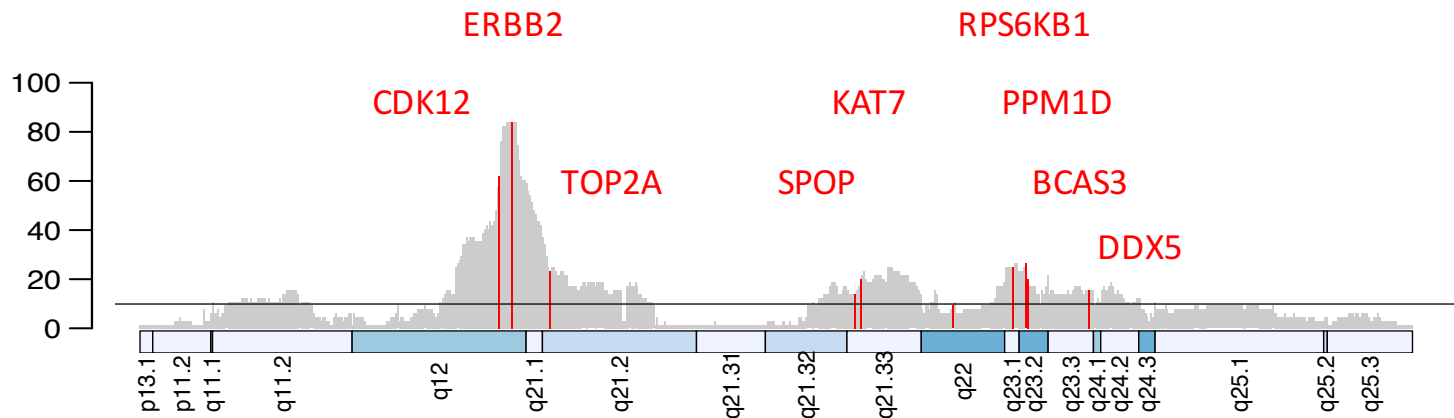
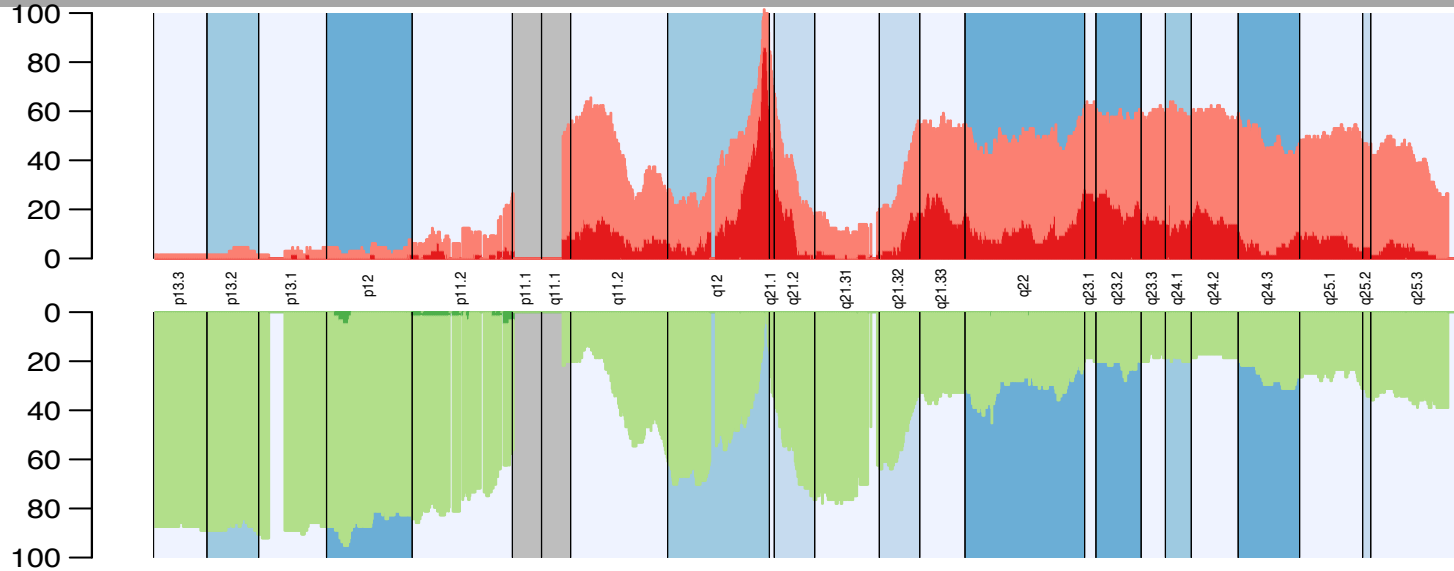
PI034

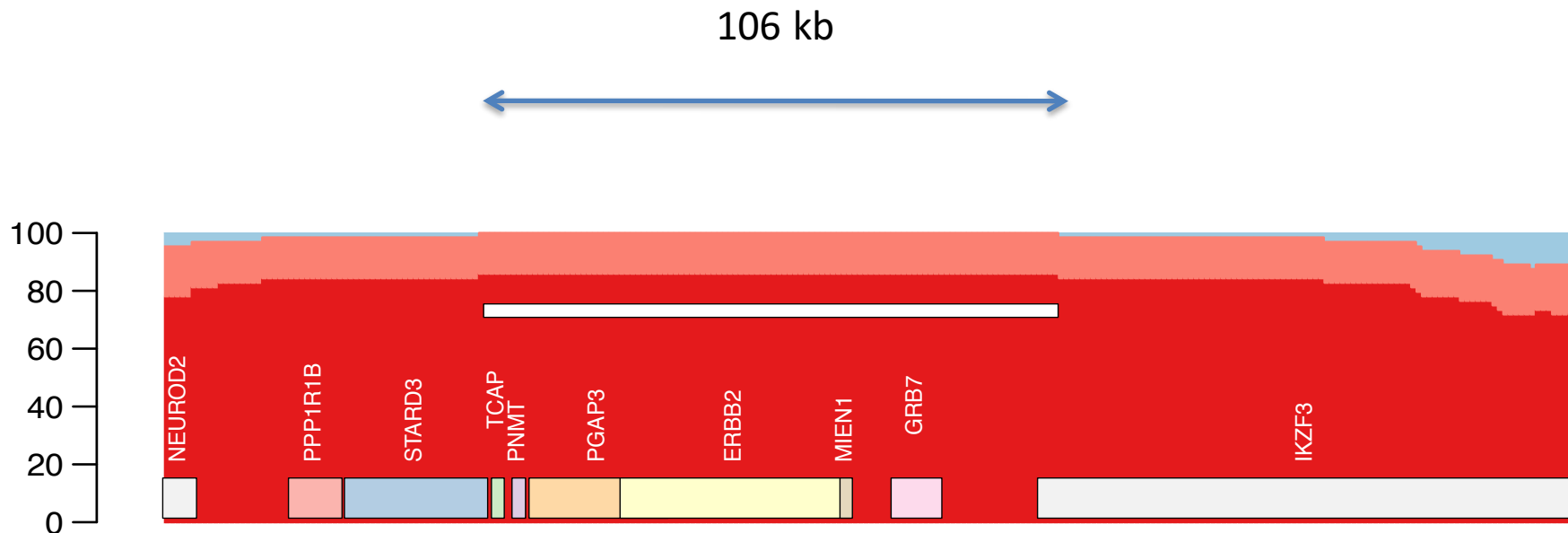


HER-positive breast cancer heterogeneity: a whole genome sequence and transcriptome perspective

Anthony Ferrari, Anne Vincent-Salomon, Xavier Pivot et al

Nature comm 2016





ARTICLE

Received 3 Dec 2015 | Accepted 12 Jun 2016 | Published 13 Jul 2016

DOI: 10.1038/ncomms12222

OPEN

A whole-genome sequence and transcriptome perspective on HER2-positive breast cancers

Anthony Ferrari¹, Anne Vincent-Salomon², Xavier Pivot³, Anne-Sophie Sertier¹, Emilie Thomas¹, Laurie Tonon¹, Sandrine Boyault⁴, Eskeatnaf Mulugeta⁵, Isabelle Treilleux⁶, Gaëtan MacGrogan⁷, Laurent Arnould⁸, Janice Kielbassa¹, Vincent Le Texier¹, Hélène Blanché⁹, Jean-François Deleuze⁹, Jocelyne Jacquemier¹⁰, Marie-Christine Mathieu¹¹, Frédérique Penault-Llorca¹², Frédéric Bibeau¹³, Odette Mariani¹⁴, Cécile Mannina¹⁵, Jean-Yves Pierga¹⁶, Olivier Trédan¹⁷, Thomas Bachelot¹⁷, Hervé Bonnefoi¹⁸, Gilles Romieu¹⁹, Pierre Fumoleau⁸, Suzette Delaloge¹¹, Maria Rios²⁰, Jean-Marc Ferrero²¹, Carole Tarpin²², Catherine Bouteille²³, Fabien Calvo²⁴, Ivo Glynné Gut^{25,26}, Marta Gut^{25,26}, Sancha Martin²⁷, Serena Nik-Zainal^{27,28}, Michael R. Stratton²⁷, Iris Pauporté²⁹, Pierre Saintigny^{30,31,32}, Daniel Birnbaum³³, Alain Viari^{1,34} & Gilles Thomas¹



ARTICLE OPEN

Constitutional variants are not associated with HER2-positive breast cancer: results from the SIGNAL/PHARE clinical cohort

Xavier Pivot¹, Gilles Romieu², Pierre Fumoleau³, Maria Rios⁴, Hervé Bonnefoi⁵, Thomas Bachelot⁶, Patrick Soulié⁷, Christelle Jouannaud⁸, Hugues Bourgeois⁹, Thierry Petit¹⁰, Isabelle Tennevet¹¹, David Assouline¹², Marie-Christine Mathieu¹³, Jean-Philippe Jacquin¹⁴, Sandrine Lavau-Denes¹⁵, Ariane Darut-Jouve¹⁶, Jean-Marc Ferrero¹⁷, Carole Tarpin¹⁸, Christelle Lévy¹⁹, Valérie Delecroix²⁰, Véronique Trillet-Lenoir²¹, Oana Cojocarasu²², Jérôme Meunier²³, Jean-Yves Pierga²⁴, Cécile Agostini²⁵, Pierre Kerbrat²⁶, Céline Faure-Mercier²⁷, Hélène Blanché²⁸, Mourad Sahbatou²⁸, Anne Boland²⁹, Delphine Bacq²⁹, Céline Besse²⁹, Fabien Calvo¹³, Alexia Renaud³⁰, Jean-François Deleuze^{28,29}, Iris Pauporté²⁷, Gilles Thomas³¹ and David G. Cox³⁰

npj Breast Cancer (2017) 3:4 ; doi:10.1038/s41523-017-0005-y

