# A Balanced Translocation Disrupting *BCL2L10* and *PNLDC1* Segregates With Affective Psychosis

Christian G. Bouwkamp,[1,2] Anneke J. A. Kievit,[2] Simone Olgiati,[2] Guido J. Breedveld,[2] Michiel Coesmans,[1] Vincenzo Bonifati,[2] and Steven A. Kushner[1]*

[1]Department of Psychiatry, Erasmus University Medical Center, Rotterdam, The Netherlands

[2]Department of Clinical Genetics, Erasmus University Medical Center, Rotterdam, The Netherlands

Affective psychoses are a group of severe psychiatric disorders, including schizoaffective disorder and bipolar I disorder, together affecting ∼1% of the population. Despite their high heritability, the molecular genetics and neurobiology of affective psychosis remain largely elusive. Here, we describe the identification of a structural genetic variant segregating with affective psychosis in a family with multiple members suffering from bipolar I disorder or schizoaffective disorder, bipolar type. A balanced translocation involving chromosomes 6 and 15 was detected by karyotyping and fluorescence in-situ hybridization (FISH). Using whole-genome sequencing, we rapidly delineated the translocation breakpoints as corresponding intragenic events disrupting *BCL2L10* and *PNLDC1*. These data warrant further consideration for *BCL2L10* and *PNLDC1* as novel candidates for affective psychosis. © 2016 The Authors. *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics* Published by Wiley Periodicals, Inc.

Key words: cytogenetics; affective psychosis; bipolar disorder; schizoaffective disorder; balanced translocation; whole-genome sequencing; *BCL2L10*; *PNLDC1*

## INTRODUCTION

Affective psychoses comprise a group of severely debilitating psychiatric disorders, including bipolar I disorder and schizoaffective disorder, together affecting ∼1% of the population [Perälä et al., 2007]. These disorders profoundly impact quality of life, including education, employment, and interpersonal relationships [Saarni et al., 2010]. The suicide rate in patients with bipolar disorder is ∼16% [Clements et al., 2013].

Bipolar disorder is well known to have a strong genetic component, with heritability estimates as high as ∼0.75 [Sullivan et al., 2012]. Despite this, the molecular genetic architecture of bipolar disorder remains largely unknown. There has been longstanding interest in the Mendelian genetics of severe mental illness using family-based linkage approaches [Baron, 2002; Badner et al., 2013] and genome-wide association studies (GWAS) [Psychiatric GWAS Consortium Bipolar Disorder Working Group, 2011]. However, replication of linkage findings in independent cohorts has generally been lacking [Lewis et al., 2003].

The emergence of next-generation sequencing (NGS), such as whole-exome sequencing and whole-genome sequencing, have enabled powerful family-based approaches for the identification of the genetic causes of disease. Here, we report the results of our investigations in a family with affective psychosis. Using traditional cytogenetic techniques followed by whole-genome sequencing, we identified a balanced translocation between the long arms of chromosomes 6 and 15, which disrupts the genes *BCL2L10* and *PNLDC1*, and segregates with affective psychosis.
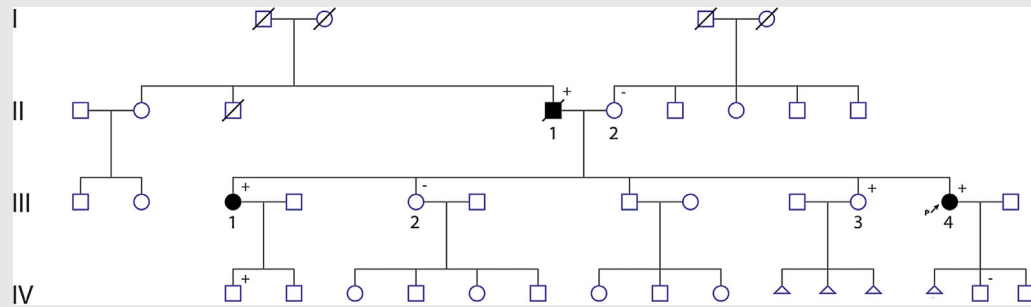
FIG. 1. Pedigree. The index patient (III-4) is indicated with an arrow as the proband (P). Shaded symbols indicate family members with affective psychosis. Subjects from whom DNA was available are numbered. Plus (+) or minus (−) symbols indicate the presence or absence of the balanced translocation.

## SUBJECTS AND METHODS

### Participants

We ascertained a Dutch family of Caucasian ethnicity with a high incidence of affective psychosis (bipolar I disorder and schizoaffective disorder, bipolar type), compatible with an autosomal dominant pattern of disease inheritance (Fig. 1). The participants were diagnosed using the structured interview for DSM-IV disorders (SCID-1). This study was performed in compliance with the Declaration of Helsinki and was approved by the medical-ethical committee of the Erasmus University Medical Center. All participants provided written informed consent.

### Cytogenetic Studies

Karyotyping was performed on metaphase chromosomes isolated from freshly cultured peripheral blood lymphocytes from the index patient (III-4). Fluorescence in-situ hybridization (FISH) analyses were performed for the index patient (III-4) on metaphase chromosomes derived from freshly cultured peripheral blood lymphocytes according to previously published methods [Pinkel et al., 1986]. Whole-chromosome-specific paints were obtained from a commercial provider (Eurodiagnostica, Malmo, Sweden). Probes were labeled with either biotin (Bio) or digoxigenin (Dig) using the Nick Labeling Kit (Roche, Basel, Switserland). Bio/Dig were detected with a one-layer amplification step using streptavidin Alexa 594 (Molecular Probes, Eugene, OR) and anti-Dig-fluorescence (Roche). Chromosomes were counterstained with Vectashield (Vector, Laboratories, Burlingame, CA) containing 4,6-diamidino-2-phenylindole (Sigma, St. Louis, MO). Images were captured using a Zeiss Axioskop II fluorescence microscope and Genetiscan Power Gene System (Applied Imaging, Grand Rapids, MI).

### Whole-Genome Sequencing

Genomic DNA was isolated from peripheral blood using standard protocols. Whole-genome sequencing was performed in the index patient (III-4) at $40\times$ average coverage depth (Fig. 1) (Complete Genomics, Mountain View, CA). After an adapter build-in step, ~400 base pair genomic fragments underwent circular PCR amplification on DNA nanoballs. Self-assembling nanoarrays with one nanoball per well were used for combinatorial probe-anchor ligation (cPAL™) to build in fluorophore-labeled dNTPs. Reads were aligned to the human reference genome version GRCh37/hg19. Mapped reads and coverage depth were used to identify single nucleotide variants (SNVs), small insertions and deletions (indels), copy number variants (CNVs), structural rearrangements, and mobile element insertions [Drmanac et al., 2010].

### Polymerase Chain Reaction (PCR) and Sanger Sequencing

The translocation breakpoint and flanking sequence were confirmed by Sanger sequencing in the DNA samples of all ascertained family members (II-1, II-2, III-1, III-2, III-3, and III-4) (Supplementary Methods, Supplementary Table SI).

### Reference Sequences

The GRCh37/hg19 build was used for annotation of the whole-genome sequencing data, design of the Sanger sequencing primers, and Sanger sequence analysis. All variants identified were annotated according to GenBank reference sequences with accession numbers for BCL2L10 (NM_020396) and PNLDC1 (NM_173516).

### RESULTS

The phenotypic profile of all ascertained family members is provided in Table I. The index patient (III-4) suffered from schizoaffective disorder, bipolar type with a history of manic-psychotic episodes, and multiple inpatient psychiatric hospital admissions. In addition, she experienced a spontaneous termination of pregnancy at age 30. She was clinically stable on a maintenance regimen of 375 mg/day quetiapine. The index patient was the youngest of five siblings, with a brother and three older sisters. Her eldest sister (III-1) was diagnosed with bipolar I disorder and maintained on 75 mg/day quetiapine with residual depressive symptoms. The second oldest sister (III-2) suffered from fibromyalgia, chronic fatigue syndrome, and

TABLE I. Clinical Characteristics

| Ped ID | II-1 | II-2 | III-1 | III-2 | III-3 | III-4 |
|---|---|---|---|---|---|---|
| t(6;15)(q26;q21) translocation carrier | Yes | No | No | Yes | Yes | Yes |
| DSM-IV Diagnosis | Bipolar I disorder | None | None | Bipolar I disorder | None | Schizoaffective disorder, bipolar type |
| Age at examination | Deceased (at age 69) | 83 | 53 | 55 | 50 | 40 |
| Age of onset depressive episodes | Unknown | | | 16 | Na | 17 |
| Number of depressive episodes | | | | >10 | | 3 |
| Age of onset manic-psychotic episodes | Unknown | | | 44 | Na | 23 |
| Number of manic-psychotic episodes | | | | 3 | | 1 |
| Medication | Unknown | Metoprolol, barnidipine, triamterene, carbasalate calcium | Fentanyl plasters, clonidine, estriadol valerate, clonazepam | Quetiapine | None | Quetiapine |
| Other diagnoses | None | Hypertension, essential thrombocythemia | Fibromyalgia, chronic fatigue syndrome, anxiety symptoms | None | Three spontaneous terminations of pregnancy | Single spontaneous termination of pregnancy |
| Educational level | Primary school | Primary school | Secondary education | Secondary education | Higher professional education | Higher professional education |

anxiety symptoms. Their brother had no significant history of psychiatric symptoms. Her youngest sister (III-3) had multiple spontaneous abortions in the first trimester of pregnancy in the setting of clomifene therapy to induce ovulation, but no significant history of psychiatric symptoms. Their father (II-1) was deceased but reported by the family as having a diagnosis of bipolar I disorder with multiple inpatient psychiatric hospitalizations. His medical records were unavailable for independent review. Their mother (II-2) had no significant psychiatric history.

Karyotyping and FISH revealed a balanced translocation in the index patient (III-4). The translocation breakpoints were localized to cytogenetic bands at 6q26 and 15q21, with a formal karyotype of 46,XX,t(6;15)(q26;q21) (Fig. 2). In order to map the precise chromosomal breakpoints, we performed whole-genome sequencing using Complete Genomics technology and confirmed by Sanger sequencing (Fig. 3). The breakpoint on chromosome 6 was located in intron 11 of *Poly(A)-specific ribonuclease (PARN)-like domain containing 1* (*PNLDC1*), which is transcribed from the forward strand t(6;15)(q26;q21)1097+1227_1097+1228. The breakpoint on chromosome 15 was located in intron 1 of the gene B-cell lymphoma 2 Like 10 (*BCL2L10*), which is transcribed from the reverse strand t(6;15)(q26;q21)538 + 1460_538 + 1461. As a consequence of this balanced translocation, the structure and expression of a single copy of both *PNLDC1* and *BCL2L10* were disrupted and predicted to result in a heterozygous loss of function.

The presence or absence of the translocation was evaluated by Sanger sequencing in all ascertained family members (Fig. 1). Individuals II-1, III-1, and III-3 were found to carry the t(6;15)(q26;q21) translocation with the identical breakpoints and flanking sequence as the index patient (III-4). In addition to the Sanger sequencing confirmation, individuals III-1 and III-3 were also found to carry the translocation by clinical diagnostic karyotyping. Individual III-1 had two sons, of which the eldest was confirmed by clinical diagnostic karyotyping to have inherited the translocation. Neither of the two children of the index patient III-4 were found to carry the translocation by clinical genetic testing.

## DISCUSSION

We identified a balanced translocation disrupting *PNLDC1* and *BCL2L10* that segregated with affective psychosis within a family across at least two generations. Independent genetic replication will be required to definitively evaluate the association of *PNLDC1* and *BCL2L10* with affective psychosis.

*BCL2L10* encodes a 204 amino acid intracellular membrane-associated BCL2 family protein which is expressed in the brain and localized to mitochondria [Zhang et al., 2001]. The BCL2L10 protein functions to negatively regulate apoptosis in the mitochondrial death pathway by preventing cytochrome c release, caspase 3 activation, and mitochondrial membrane potential collapse [Zhang et al., 2001; Cory and Adams, 2002]. A previous study
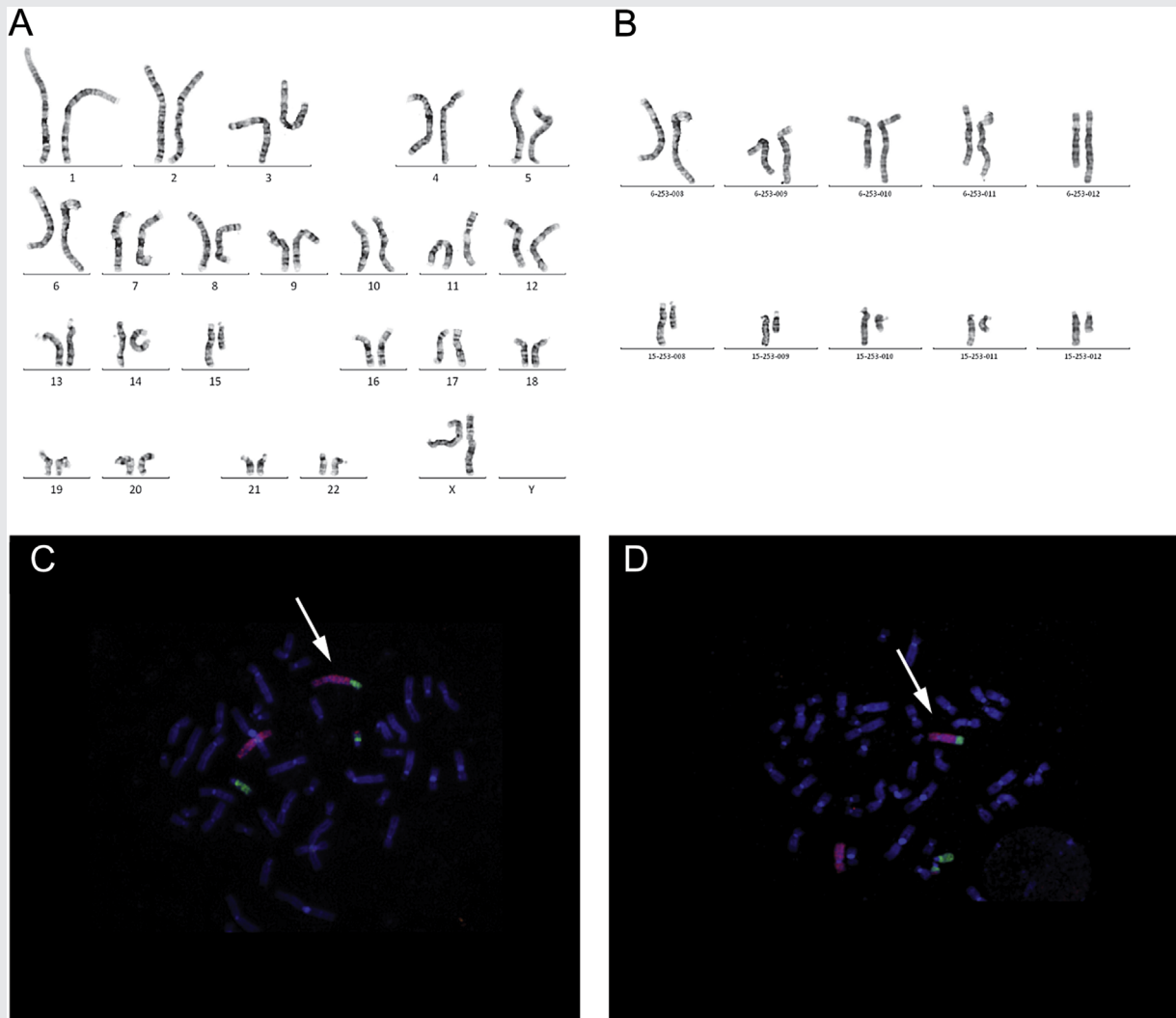
FIG. 2. Cytogenetic studies. (A) Complete karyogram from subject III-4 with the inherited balanced translocation: 46,XX,t(6;15)(q26;q21). (B) Selected karyogram images demonstrating the heterozygous abnormal representation of chromosome 6 (top row) and chromosome 15 (bottom row). (C and D) Fluorescence in-situ hybridization showing the abnormalities in chromosome 6 (C) and chromosome 15 (D) indicated by the arrows. In (C), probes pertaining to chromosome 6 are labeled in red, and probes pertaining to chromosome 15 are labeled in green. In (D), probes pertaining to chromosome 15 are labeled in red, and probes pertaining to chromosome 6 are labeled in green. For both (C) and (D), chromosomes are visualized in blue.

using array-based expression analysis identified alterations of an apoptosis-related gene set in lithium-responsive patients with unipolar depression [Lowthert et al., 2012]. Notably, anti-apoptotic BCL2 family transcripts, of which BCL2L10 is a member, were upregulated while pro-apoptotic family members were downregulated in the lithium responsive group. Analogously, the apoptotic regulatory function of BCL2L10 may also have contributed to the occurrence of multiple spontaneous abortions in family members carrying the *BCL2L10* disruption, as two different studies have confirmed high expression levels of this gene in human oocytes for which abnormal subcellular localization of BCL2L10 was associated with poor-quality embryos during preimplantation screening [Guillemin et al., 2009; Yoon et al., 2009; Guérin et al., 2013].

However, an important and non-mutually exclusive possibility is that the spontaneous abortions are a consequence of embryos inheriting an unbalanced translocation leading to aneuploidy as a result of meiosis involving the maternal translocation [Tharapel et al., 1985].

The other gene disrupted by the balanced translocation, *PNLDC1*, encodes a 520 amino acid protein containing an RNaseH-like domain and RNAse_CAF1 domain. The poly(A)-specific ribonuclease group of proteins are involved in deadenylation of mRNA in eurkaryotes, thereby regulating mRNA levels and translation. However, the function of the nuclease-containing PARN-like protein PNLDC1 has not been investigated [Virtanen et al., 2013].
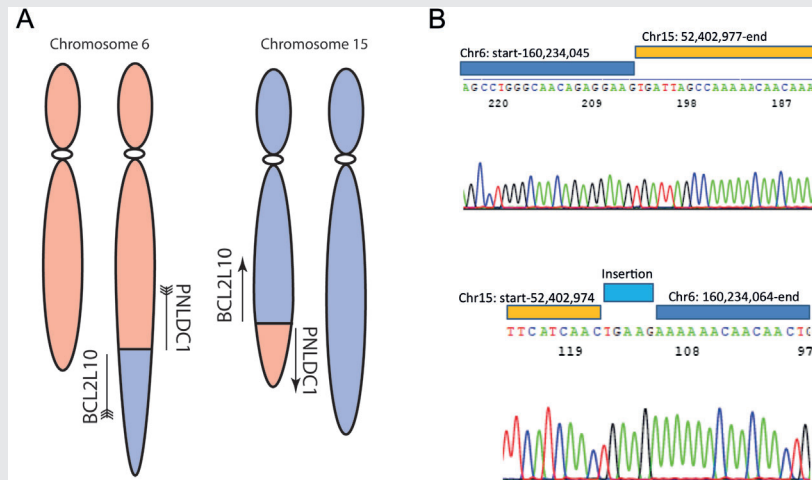
**FIG. 3.** Chromosomal rearrangement. (A) Schematic view of the balanced translocation involving chromosomes 6 and 15. (B) Electropherograms of the DNA sequence across the translocation breakpoints.

To our knowledge, there is currently no evidence for linkage with affective psychosis in the regions surrounding BCL2L10 or PNLDC1, nor for common variants to be associated with affective psychosis, based on the data in the Johns Hopkins Metamoodics database for genome-wide linkage which comprises 972 families with bipolar disorder and schizoaffective disorder and GWAS data of bipolar disorder comprising 7,616 cases and 10,340 controls [Seifuddin et al., 2012; Pirooznia et al., 2014]. In addition, the GWAS dataset from the Psychiatric Genomics Consortium of 11,974 cases and 51,792 controls provides no clear evidence of common alleles in these regions associated with bipolar disorder [Psychiatric GWAS Consortium Bipolar Disorder Working Group, 2011]. Furthermore, genome-wide exome sequencing studies are not yet publically available for bipolar disorder to examine the presence of rare exonic variants in these regions.

Although schizophrenia is a form of non-affective psychosis, multiple CNVs have been identified which increase the risk of schizophrenia and bipolar disorder [Rodriguez-Murillo et al., 2012; Green et al., 2016]. Therefore, we examined the data available from the recently published Sweden Schizophrenia Exome study which involved whole-exome sequencing of 2,536 patients with schizophrenia and 2,543 unaffected controls [Purcell et al., 2014]. In BCL2L10, only a single rare coding variant was identified in the entire cohort (c.467G>A, p.W156*, MAF<0.005, nonsynonymous), which was found in one patient and no controls. In PNLDC1, two coding variants were identified: c.13 C>T, p.R5* present in one patient and one control (within transcript NM_001271862, the effect of this variant is c.77–31 C>T), and c.244 C>T, p.L82F (NM_001271862: c.277 C>T p.L93F in) present in one patient and two controls. This scenario illustrates the difficulties in conclusively establishing a disease-causing role for very rare disease-associated variants. Longitudinal follow-up studies of this family, in addition to continued screening of other probands and case/control cohorts for rare coding variants in these genes, have the potential to provide further clarity regarding the pathophysiology of affective psychosis.

The study of patients who carry rare cytogenetic abnormalities has long been an important strategy for the identification of candidate disease-causing genes, including the first reported candidate gene for psychosis (DISC1) [MacIntyre et al., 2003]. Although highly penetrant mutations are rare causes of psychiatric disorders, their identification have the potential to highlight molecular pathways that are mechanistically involved in disease pathogenesis among the wider group of patients who do not carry high-penetrance mutations. Prominent examples for brain diseases with an otherwise complex genetic architecture include the identification of mutations in the gene coding for amyloid precursor protein (APP) for Alzheimer's disease [Goate et al., 1991; Kamino et al., 1992; Tanzi et al., 1992] and the gene encoding alpha-synuclein (SNCA) in Parkinson's disease and dementia with Lewy bodies [Polymeropoulos et al., 1996]. Therefore, we believe that family-based genetic studies coupled with next-generation DNA sequencing technologies hold considerable potential to contribute to the understanding of the neurobiological underpinnings of severe psychiatric illness.

## REFERENCES

Badner JA, Koller D, Foroud T, Edenberg H, Nurnberger JI, Zandi PP, Willour VL, Mcmahon FJ, Potash JB, Grozeva D, Green E, Kirov G, Jones I, Jones L. 2013. Genome wide linkage analysis of 972 bipolar

pedigrees using single nucleotide polymorphisms. Mol Psychiatry 17:818–826.

Baron M. 2002. Manic-depression genes and the new millennium: Poised for discovery. Mol Psychiatry 7:342–358.

Clements C, Morriss R, Jones S, Peters S, Roberts C, Kapur N. 2013. Suicide in bipolar disorder in a national English sample, 1996–2009: Frequency, trends and characteristics. Psychol Med 43:2593–2602.

Cory S, Adams JM. 2002. The Bcl2 family: Regulators of the cellular life-or-death switch. Nat Rev Cancer 2:647–656.

Drmanac R, Sparks AB, Callow MJ, Halpern AL, Burns NL, Kermani BG, Carnevali P, Nazarenko I, Nilsen GB, Yeung G, Dahl F, Fernandez A, Staker B, Pant KP, Baccash J, Borcherding AP, Brownley A, Cedeno R, Chen L, Chernikoff D, Cheung A, Chirita R, Curson B, Ebert JC, Hacker CR, Hartlage R, Hauser B, Huang S, Jiang Y, Karpinchyk V, Koenig M, Kong C, Landers T, Le C, Liu J, McBride CE, Morenzoni M, Morey RE, Mutch K, Perazich H, Perry K, Peters BA, Peterson J, Pethiyagoda CL, Pothuraju K, Richter C, Rosenbaum AM, Roy S, Shafto J, Sharanhovich U, Shannon KW, Sheppy CG, Sun M, Thakuria JV, Tran A, Vu D, Zaranek AW, Wu X, Drmanac S, Oliphant AR, Banyai WC, Martin B, Ballinger DG, Church GM, Reid CA. 2010. Human genome sequencing using unchained base reads on self-assembling DNA nanoarrays. Science 327:78–81.

Goate A, Chartier-Harlin MC, Mullan M, Brown J, Crawford F, Fidani L, Giuffra L, Haynes A, Irving N, James L. 1991. Segregation of a missense mutation in the amyloid precursor protein gene with familial Alzheimer's disease. Nature 349:704–706.

Green EK, Rees E, Walters JTR, Smith K-G, Forty L, Grozeva D, Moran JL, Sklar P, Ripke S, Chambert KD, Genovese G, McCarroll SA, Jones I, Jones L, Owen MJ, O'Donovan MC, Craddock N, Kirov G. 2016. Copy number variation in bipolar disorder. Mol Psychiatry 21:89–93.

Guérin J-F, Cornut-Thibaut A, Giscard-Destaing S, Pouvreau S, Guillemin Y, Aouacheria A. 2013. Subcellular dynamics of the maternal cell death regulator BCL2L10 in human preimplantation embryos. Hum Reprod 28:729–739.

Guillemin Y, Lalle P, Gillet G, Guerin J-F, Hamamah S, Aouacheria A. 2009. Oocytes and early embryos selectively express the survival factor BCL2L10. J Mol Med (Berl) 87:923–940.

Kamino K, Orr HT, Payami H, Wijsman EM, Alonso ME, Pulst SM, Anderson L, O'dahl S, Nemens E, White JA. 1992. Linkage and mutational analysis of familial Alzheimer disease kindreds for the APP gene region. Am J Hum Genet 51:998–1014.

Lewis CM, Levinson DF, Wise LH, DeLisi LE, Straub RE, Hovatta I, Williams NM, Schwab SG, Pulver AE, Faraone SV, Brzustowicz LM, Kaufmann CA, Garver DL, Gurling HMD, Lindholm E, Coon H, Moises HW, Byerley W, Shaw SH, Mesen A, Sherrington R, O'Neill FA, Walsh D, Kendler KS, Ekelund J, Paunio T, Lönnqvist J, Peltonen L, O'Donovan MC, Owen MJ, Wildenauer DB, Maier W, Nestadt G, Blouin J-L, Antonarakis SE, Mowry BJ, Silverman JM, Crowe RR, Cloninger CR, Tsuang MT, Malaspina D, Harkavy-Friedman JM, Svrakic DM, Bassett AS, Holcomb J, Kalsi G, McQuillin A, Brynjolfson J, Sigmundsson T, Petursson H, Jazin E, Zoëga T, Helgason T. 2003. Genome scan meta-analysis of schizophrenia and bipolar disorder, part II: Schizophrenia. Am J Hum Genet 73:34–48.

Lowthert L, Leffert J, Lin A, Umlauf S, Maloney K, Muralidharan A, Lorberg B, Mane S, Zhao H, Sinha R, Bhagwagar Z, Beech R. 2012. Increased ratio of anti-apoptotic to pro-apoptotic Bcl2 gene-family members in lithium-responders one month after treatment initiation. Biol Mood Anxiety Disord 2:15.

MacIntyre DJ, Blackwood DHR, Porteous DJ, Pickard BS, Muir WJ. 2003. Chromosomal abnormalities and mental illness. Mol Psychiatry 8:275–287.

Perälä J, Suvisaari J, Saarni SI, Kuoppasalmi K, Isometsä E, Pirkola S, Partonen T, Tuulio-Henriksson A, Hintikka J, Kieseppä T, Härkänen T, Koskinen S, Lönnqvist J. 2007. Lifetime prevalence of psychotic and bipolar I disorders in a general population. Arch Gen Psychiatry 64:19.

Pinkel D, Straume T, Gray JW. 1986. Cytogenetic analysis using quantitative, high-sensitivity, fluorescence hybridization. Proc Natl Acad Sci USA 83:2934–2938.

Pirooznia M, Seifuddin F, Judy J, Goes FS, Potash JB, Zandi PP. 2014. Metamoodics: Meta-analysis and bioinformatics resource for mood disorders. Mol Psychiatry 19:748–749.

Polymeropoulos MH, Higgins JJ, Golbe LI, Johnson WG, Ide SE, Di Iorio G, Sanges G, Stenroos ES, Pho LT, Schaffer AA, Lazzarini AM, Nussbaum RL, Duvoisin RC. 1996. Mapping of a gene for Parkinson's disease to chromosome 4q21-q23. Science 274:1197–1199.

Psychiatric GWAS Consortium Bipolar Disorder Working Group. 2011. Large-scale genome-wide association analysis of bipolar disorder identifies a new susceptibility locus near ODZ4. Nat Genet 43:977–983.

Purcell SM, Moran JL, Fromer M, Ruderfer D, Solovieff N, Roussos P, O&apos, Dushlaine C, Chambert K, Bergen SE, Kähler A, Duncan L, Stahl E, Genovese G, Fernández E, Collins MO, Komiyama NH, Choudhary JS, Magnusson PKE, Banks E, Shakir K, Garimella K, Fennell T, DePristo M, Grant SGN, Haggarty SJ, Gabriel S, Scolnick EM, Lander ES, Hultman CM, Sullivan PF, McCarroll SA, Sklar P. 2014. A polygenic burden of rare disruptive mutations in schizophrenia. Nature 506:185–190.

Rodriguez-Murillo L, Gogos JA, Karayiorgou M. 2012. The genetic architecture of schizophrenia: New mutations and emerging paradigms. Annu Rev Med 63:63–80.

Saarni SI, Viertiö S, Perälä J, Koskinen S, Lönnqvist J, Suvisaari J. 2010. Quality of life of people with schizophrenia, bipolar disorder and other psychotic disorders. Br J Psychiatry 197:386–394.

Seifuddin F, Mahon PB, Judy J, Pirooznia M, Jancic D, Taylor J, Goes FS, Potash JB, Zandi PP. 2012. Meta-analysis of genetic association studies on bipolar disorder. Am J Med Genet B Neuropsychiatr Genet 159B:508–518.

Sullivan PF, Daly MJ, O'Donovan M. 2012. Genetic architectures of psychiatric disorders: The emerging picture and its implications. Nat Rev Genet 13:537–551.

Tanzi RE, Vaula G, Romano DM, Mortilla M, Huang TL, Tupler RG, Wasco W, Hyman BT, Haines JL, Jenkins BJ. 1992. Assessment of amyloid beta-protein precursor gene mutations in a large set of familial and sporadic Alzheimer disease cases. Am J Hum Genet 51:273–282.

Tharapel AT, Tharapel SA, Bannerman RM. 1985. Recurrent pregnancy losses and parental chromosome abnormalities: A review. Br J Obstet Gynaecol 92:899–914.

Virtanen A, Henriksson N, Nilsson P, Nissbeck M. 2013. Poly(A)-specific ribonuclease (PARN): An allosterically regulated, processive and mRNA cap-interacting deadenylase. Crit Rev Biochem Mol Biol 48:192–209.

Yoon S-J, Kim E-Y, Kim YS, Lee H-S, Kim K-H, Bae J, Lee K-A. 2009. Role of Bcl2-like 10 (Bcl2l10) in regulating mouse oocyte maturation. Biol Reprod 81:497–506.

Zhang H, Holzgreve W, De Geyter C. 2001. Bcl2-L-10, a novel anti-apoptotic member of the Bcl-2 family, blocks apoptosis in the mitochondria death pathway but not in the death receptor pathway. Hum Mol Genet 10:2329–2339.

## SUPPORTING INFORMATION

Additional supporting information may be found in the online version of this article at the publisher's web-site.