

## **Acta Neuropathologica**

### **Germline and somatic FGFR1 abnormalities in dysembryoplastic neuroepithelial tumors**

Barbara Rivera<sup>1,2</sup> · Tenzin Gayden<sup>2</sup> · Jian Carrot-Zhang<sup>2,3</sup> · Javad Nadaf<sup>2,3</sup> · Talia Boshari<sup>4</sup> · Damien Faury<sup>2</sup> · Michele Zeinieh<sup>2</sup> · Romeo Blanc<sup>5</sup> · David L. Burk<sup>6</sup> · Somayyeh Fahiminiya<sup>2,3</sup> · Eric Bareke<sup>2,3</sup> · Ulrich Schüller<sup>7</sup> · Camelia M. Monoranu,<sup>8</sup> Ronald Sträter<sup>9</sup> · Kornelius Kerl<sup>9</sup> · Thomas Niederstadt<sup>10</sup> · Gerhard Kurlemann<sup>11</sup> · Benjamin Ellezam<sup>12</sup> · Zuzanna Michalak<sup>13,14</sup> · Maria Thom<sup>13,14</sup> · Paul J. Lockhart<sup>15,16</sup> · Richard J. Leventer<sup>15,17,18</sup> · Milou Ohm<sup>19</sup> · Duncan MacGregor<sup>20</sup> · David Jones<sup>21,22</sup> · Jason Karamchandani<sup>23</sup> · Celia MT Greenwood<sup>2,24</sup> · Albert M. Berghuis<sup>6</sup> · Susanne Bens<sup>25</sup> · Reiner Siebert<sup>25</sup> · Magdalena Zakrzewska<sup>26</sup> · Pawel P. Liberski<sup>26</sup> · Krzysztof Zakrzewski<sup>27</sup> · Sanjay M. Sisodiya<sup>14,28</sup> · Werner Paulus<sup>29</sup> · Steffen Albrecht<sup>30</sup> · Martin Hasselblatt<sup>29</sup> · Nada Jabado<sup>2,31</sup> · William D Foulkes<sup>1,2,4,32</sup> · Jacek Majewski<sup>2,3</sup>

<sup>1</sup>Program in Cancer Genetics, Department of Oncology and Human Genetics, McGill University, Montreal, Quebec, Canada

<sup>2</sup>Department of Human Genetics, McGill University, Montreal, Quebec, Canada

<sup>3</sup>McGill University and Génome Québec Innovation Centre, Montreal, Quebec, Canada; <sup>4</sup>Department of Medical Genetics, Lady Davis Institute and Segal Cancer Centre, Jewish General Hospital, McGill University, Montreal, Quebec, Canada.

<sup>5</sup>Bloomfield Center for Research on Aging, Lady Davis Institute for Medical Research, McGill University, Jewish General Hospital, Montréal, Quebec, Canada

<sup>6</sup>Department of Biochemistry and Groupe de Recherche Axé sur la Structure des Protéines, McGill University, Montreal, Quebec, Canada

<sup>7</sup>Center for Neuropathology, Ludwig-Maximilians-University, Munich, Germany

<sup>8</sup>Department of Neuropathology, Institute of Pathology, University of Würzburg, Comprehensive Cancer Center Mainfranken, Würzburg, Germany

<sup>9</sup>Pediatric Hematology and Oncology, University Children's Hospital Münster, Münster, Germany

- <sup>10</sup>Department of Radiology, University Hospital Münster, Münster, Germany
- <sup>11</sup>Division of Pediatric Neurology, University Children's Hospital, Münster, Germany
- <sup>12</sup>Department of Pathology, CHU Sainte-Justine, Montreal, Canada
- <sup>13</sup>Division of Neuropathology, UCL Institute of Neurology, London, UK
- <sup>14</sup>Department of Clinical and Experimental Epilepsy, UCL Institute of Neurology, London, UK
- <sup>15</sup>Department of Pediatrics, The University of Melbourne, Melbourne, Australia
- <sup>16</sup>Bruce Lefroy Centre for Genetic Health Research, Murdoch Childrens Research Institute, Melbourne, Australia
- <sup>17</sup>Department of Neurology, The Royal Children's Hospital, Melbourne, Australia
- <sup>18</sup>Murdoch Childrens Research Institute, Melbourne, Australia
- <sup>19</sup>VUMC School of Medical Sciences, Amsterdam, The Netherlands
- <sup>20</sup>Department of Anatomical Pathology, Royal Children's Hospital, Melbourne, Australia; <sup>21</sup>German Cancer Consortium (DKTK), German Cancer Research Center (DKFZ), Heidelberg, Germany
- <sup>22</sup>Division of Pediatric Neurooncology (B062), German Cancer Research Center (DKFZ), Heidelberg, Germany
- <sup>23</sup>Department of Pathology, McGill University, Montreal Neurological Institute, Montreal, Quebec, Canada
- <sup>24</sup>Departments of Oncology and Epidemiology, Biostatistics & Occupational Health, McGill University, Montreal, Quebec, Canada
- <sup>25</sup>Institute of Human Genetics, Christian-Albrechts-University Kiel & University Hospital Schleswig-Holstein, Campus Kiel, Kiel, Germany
- <sup>26</sup>Department of Molecular Pathology and Neuropathology, Medical University of Lodz, Lodz, Poland
- <sup>27</sup>Department of Neurosurgery, Polish Mother's Memorial Hospital Research Institute, Lodz, Poland
- <sup>28</sup>Epilepsy Society, Bucks, UK
- <sup>29</sup>Institute of Neuropathology, University Hospital Münster, Münster, Germany
- <sup>30</sup>Department of Pathology, Montreal Children's Hospital, McGill University Health Centre, McGill University, Montreal, Quebec, Canada

<sup>31</sup>Department of Pediatrics, Montreal Children's Hospital, McGill University Health Centre, Montreal, Quebec, Canada

<sup>32</sup>Department of Medical Genetics and Cancer Research Program, Research Institute McGill University Health Centre, Montreal, Quebec, Canada

Correspondence to: Martin Hasselblatt, William D Foulkes or Jacek Majewski

[martin.hasselblatt@ukmuenster.de](mailto:martin.hasselblatt@ukmuenster.de), [william.foulkes@mcgill.ca](mailto:william.foulkes@mcgill.ca), [jacek.majewski@mcgill.ca](mailto:jacek.majewski@mcgill.ca)

**Suppl. Table 2a Significantly mutated genes in 40 sporadic DNET samples**

Gene	Rank	Fisher's p value	Q value	Num case mutated	Num case	Num control mutated	Num control
FGFR1*	1	3.22E-10	5.02E-08	9	40	7	1092
GPR116	2	0.001218472	0.095040819	2	40	0	1092
MTPP	3	0.002965619	0.126957774	3	40	6	1092
CAMKV	4	0.005544323	0.126957774	3	40	8	1092
HAT1	5	0.006987059	0.126957774	2	40	2	1092
PSAPL1	6	0.006987059	0.126957774	2	40	2	1092
SYDE2	7	0.007212223	0.126957774	3	40	9	1092
COL8A1	8	0.007212223	0.126957774	3	40	9	1092
SLC14A1	9	0.011385188	0.126957774	2	40	3	1092
FAM216A	10	0.011385188	0.126957774	2	40	3	1092
TSEN2	11	0.011385188	0.126957774	2	40	3	1092
MS4A4A	12	0.011385188	0.126957774	2	40	3	1092
MIER3	13	0.011385188	0.126957774	2	40	3	1092
PLD4	14	0.011393646	0.126957774	4	40	22	1092
APCDD1	15	0.01669748	0.140875479	2	40	4	1092
ZNF514	16	0.01669748	0.140875479	2	40	4	1092
SPTBN1	17	0.019712761	0.140875479	3	40	14	1092
PRMT3	18	0.022857097	0.140875479	2	40	5	1092
USP2	19	0.022857097	0.140875479	2	40	5	1092
ZNF571	20	0.022857097	0.140875479	2	40	5	1092
ANO5	21	0.022857097	0.140875479	2	40	5	1092
KRTAP10-1	22	0.022857097	0.140875479	2	40	5	1092
PKLR	23	0.022857097	0.140875479	2	40	5	1092
FREM1	24	0.023082603	0.140875479	3	40	15	1092
CPEB2	25	0.026747759	0.140875479	3	40	16	1092
ZNF354A	26	0.029800582	0.140875479	2	40	6	1092
FAM173A	27	0.029800582	0.140875479	2	40	6	1092
MFN1	28	0.029800582	0.140875479	2	40	6	1092
LRP2BP	29	0.029800582	0.140875479	2	40	6	1092
RBM15B	30	0.029800582	0.140875479	2	40	6	1092
DENND3	31	0.029800582	0.140875479	2	40	6	1092
FOXJ3	32	0.029800582	0.140875479	2	40	6	1092
P2RX2	33	0.029800582	0.140875479	2	40	6	1092
DYNC2LI1	34	0.037467714	0.16238667	2	40	7	1092
SNX29	35	0.037467714	0.16238667	2	40	7	1092
REST	36	0.045801368	0.16238667	2	40	8	1092
TNIK	37	0.045801368	0.16238667	2	40	8	1092
CCNK	38	0.045801368	0.16238667	2	40	8	1092
SYTL1	39	0.045801368	0.16238667	2	40	8	1092

Gene	Rank	Fisher's p value	Q value	Num case mutated	Num case	Num control mutated	Num control
OTUD7B	40	0.045801368	0.16238667	2	40	8	1092
PCDHGB6	41	0.045801368	0.16238667	2	40	8	1092
INPP5F	42	0.045801368	0.16238667	2	40	8	1092
ARHGAP29	43	0.045801368	0.16238667	2	40	8	1092
ASPH	44	0.045801368	0.16238667	2	40	8	1092
BCORL1^	83	0.154065807	0.340377946	2	40	17	1092
FAT1^	136	0.753908677	0.827992188	2	40	69	1092
NOTCH3^	143	0.664239474	0.751223214	2	40	58	1092

Cancer panel genes are indicated as follows:

\*FoundationOne+Neuro-Oncology

^FoundationOne

**Table S2b Variants identified in cancer-related genes from Table S2a**

Position	Variation	Ref	Alt	Cases affected	Case number	Gene	Protein change	Polyphen 2 score	Mutation Taster Score
chrX:12914748 1	nonsynonymous SNV	G	A	1	15	BCORL 1	p.V245I	0.006	0
chrX:12914960 4	frameshift deletion	AT	A	1	64	BCORL 1	p.S953fs		
chr4:18751804 7	nonsynonymous SNV	G	C	1	47	FAT1	p.P4216 R	0.467	0.959
chr4:18762990 0	nonsynonymous SNV	T	C	1	57	FAT1	p.K361R	0.003	0.954
chr19:1528496 4	nonsynonymous SNV	C	A	1	41	NOTCH 3	p.G1551 C	1	1
chr19:1529809 8	nonsynonymous SNV	G	C	1	52	NOTCH 3	p.P553R	1	1