Sir,

Martínez-Juárez et al. [2014] reported 2 siblings with trisomy 2p caused by maternal translocation t(2;12) (p22.3q24.3). Neither of these siblings nor several other patients with pure trisomy 2p cited by these authors had congenital diaphragmatic hernia (CDH), neuroblastoma or neural tube defects (NTD). Almost 20 years ago, we [Lurie et al., 1995] suggested that these findings are causally related to trisomy 2p. Martínez-Juárez et al. state that our conclusion was false and that these findings actually are caused by associated chromosomal imbalances.

CDH was reported in 7 patients with trisomy 2p (table 1). Four of these patients had associated deletions for other chromosomes, 1 had mosaic trisomy for the whole 2p and proximal part of 2q (from centromere to 2q11.2) [Kan et al., 2014], and 2 had pure trisomy 2p [Heathcote et al., 1991; Blassnig-Ezeh et al., 2013]. In the latter observation, absence of any associated imbalance was confirmed by molecular methods. Blassnig-Ezeh et al. [2013] narrowed down the critical segment for CDH to approximately 8 Mb (between 42.3 and 50.0 Mb) on 2p21. In that context, there are no reasons to relate the origin of CDH to any chromosomal abnormalities that accompanied trisomy 2p.

Table 1. CDH in individuals with partial trisomy 2p

<table>
<thead>
<tr>
<th>Reference</th>
<th>Trisomic segment</th>
<th>Associated imbalance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kan et al., 2014</td>
<td>2cen–pter (mosaic)</td>
<td>dup 2cen–q11.2 (mosaic)</td>
</tr>
<tr>
<td>Sarda et al., 1992</td>
<td>2p13pter</td>
<td>del Xp13pter</td>
</tr>
<tr>
<td>Blassnig-Ezeh et al., 2013</td>
<td>2p16.3pter</td>
<td></td>
</tr>
<tr>
<td>Mosca et al., 2011</td>
<td>2p16.3pter</td>
<td>del 15q26.2qter</td>
</tr>
<tr>
<td>Heathcote et al., 1991</td>
<td>2p21p25</td>
<td></td>
</tr>
<tr>
<td>León Leon et al., 2011</td>
<td>2p21pter</td>
<td>del 18p11pter</td>
</tr>
<tr>
<td>Bender et al., 1969</td>
<td>2p23pter</td>
<td>del 6p25pter</td>
</tr>
</tbody>
</table>

Table 2. Neuroblastoma in individuals with partial trisomy 2p

<table>
<thead>
<tr>
<th>Reference</th>
<th>Trisomic segment</th>
<th>Associated imbalance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Say et al., 1980</td>
<td>2p21p25</td>
<td></td>
</tr>
<tr>
<td>Dowa et al., 2006</td>
<td>2p21pter</td>
<td>del 8p23.2pter</td>
</tr>
<tr>
<td>Stephane et al., 2003</td>
<td>2p22pter</td>
<td>del 8p23pter</td>
</tr>
<tr>
<td>Nagano et al., 1980</td>
<td>2p22.3pter</td>
<td>del 16p13.3pter</td>
</tr>
<tr>
<td>Patel et al., 1997</td>
<td>2p23pter</td>
<td>del 13q34pter</td>
</tr>
<tr>
<td>Yüksel et al., 2002</td>
<td>2p23pter</td>
<td>del 17q25pter</td>
</tr>
<tr>
<td>Morgenstern et al., 2014</td>
<td>2p23pter</td>
<td>del 16p13.3pter</td>
</tr>
<tr>
<td>Nowaczyk et al., 2000</td>
<td>2p23.2pter</td>
<td>del 7q36.1pter</td>
</tr>
<tr>
<td>Warad et al., 2012</td>
<td>2p24.1p25.3</td>
<td></td>
</tr>
<tr>
<td>Lipska et al., 2013</td>
<td>2p24.1pter</td>
<td>del 18q22.3qter</td>
</tr>
<tr>
<td>Van Mater et al., 2013</td>
<td>2p24.3 (1 Mb)</td>
<td>del 3q29 (0.144 Mb)</td>
</tr>
</tbody>
</table>
At least 11 patients with trisomy 2p developed neuroblastoma (table 2). Two of these patients had pure trisomy 2p [Say et al., 1980; Warad et al., 2012], another had an additional 0.144-Mb duplication of 3q29 and a 0.219-Mb deletion of 20p12.1 [Van Mater et al., 2013]. In the opinion of Martínez-Juárez et al. [2014], a person with an imbalance of this size may be classified as pure duplication 2p. Eight others had an associated imbalance. New data show that duplication of the \textit{MYCN} locus at 2p24.3 is responsible for the origin of neuroblastoma in patients with trisomy 2p [Lipska et al., 2013].

NTD were found in 20 published patients with trisomy 2p (table 3). There are no other partial trisomies where NTD were reported in such a large number of persons. In at least 3 patients [Therkelsen et al., 1973; Thangavelu et al., 2004], anencephaly or spina bifida was found without any associated imbalance.

Of course, several reports of the above-mentioned abnormalities in individuals with pure trisomy 2p were published in the 'pre-molecular era', and a tiny associated imbalance for other chromosomal segments could not be completely excluded. However, neither of the partial monosomies associated with neuroblastoma (deletions of the distal parts of 7q, 8p, 13q, 16p, 17q, or 18q) are known as causative factors for the origin of this tumor. The same is true for partial monosomies in patients with trisomy 2p and NTD, because these deletions (with the exception of del 13q) are not known as being associated with anencephaly or spina bifida. These facts suggest that trisomy 2p itself but not the associated imbalances are responsible for the origin of NTD.

So, there is strong evidence that all 3 groups of the above-mentioned defects are caused by trisomy 2p, but not by the associated imbalance.

Martínez-Juárez et al. [2014] state that a horseshoe kidney observed in one of their patients is a 'previously unrecognized defect associated with this syndrome'. Actually, however, horseshoe kidney was reported both in patients with pure trisomy 2p [Cummings et al., 1997] and in association with another imbalance [Larson et al., 1982].

Also, both siblings reported by Martínez-Juárez et al. [2014] were presented by Quintana Palma et al. [2010] at the 35th annual meeting of the Mexican Society of Human Genetics. The published abstract of their presentation states that the boy had unilateral renal agenesis and hypospadias (although in the article they describe these defects as horseshoe kidney and overriding scrotum).

Precise description of the phenotype, thorough and critical review of the literature, as well as care in drawn conclusions are important issues to consider in the writing of any scientific paper.

\begin{table}[h]
\centering
\caption{NTD in individuals with partial trisomy 2p}
\begin{tabular}{|l|l|l|l|}
\hline
Reference & Trisomic segment & Associated imbalance & Type of defect \\
\hline
Therkelsen et al., 1973 & 2p13p24 & – & spina bifida \\
Fineman et al., 1983 & 2p13pter & del 9p24pter & spina bifida \\
Walbaum et al., 1984 & 2p13pter & del 5p15pter & anencephaly \\
Sarda et al., 1992 & 2p13pter & del Xp13pter & spina bifida \\
Mosca et al., 2011 & 2p16.3pter & del 15q26.2qter & spina bifida \\
Hahm et al., 1999 & 2p21pter & del 15q26qter & anencephaly, spina bifida \\
Kim et al., 2007 & 2p21pter & del 5p15pter & exencephaly \\
Thangavelu et al., 2004, case 1 & 2p22p25 & – & anencephaly \\
Thangavelu et al., 2004, case 2 & 2p22p25.3 & – & anencephaly \\
Doray et al., 2003, case 1 & 2p22pter & del 15q26qter & anencephaly, spina bifida \\
Doray et al., 2003, case 2 & 2p22pter & del 15q26qter & anencephaly \\
Winsor et al., 1997, case 1 & 2p23pter & del 5p15pter & anencephaly \\
Winsor et al., 1997, case 2 & 2p23pter & del 5p15pter & anencephaly \\
Stallworth et al., 2008 & 2p23pter & del 9p24pter & anencephaly, spina bifida \\
Wellesley and Boyle, 2000 & 2p23.1pter & del 3q29qter & anencephaly, spina bifida \\
Singer et al., 1987 & 2p24pter & del 10q26qter & anencephaly \\
Cain et al., 2008 & 2p25.1pter & del 13q32qter & occipital encephalocele \\
Gregory et al., 2000, case 1 & 2p25.2pter & del 10q26.3qter & anencephaly \\
Gregory et al., 2000, case 2 & 2p25.2pter & del 10q26.3qter & anencephaly \\
Poulose et al., 2007 & 2p25.2pter & del 10q26.3qter & 'exencephaly-anencephaly' \\
\hline
\end{tabular}
\end{table}
References

Bender K, Reinwein H, Gorman LZ, Wolf U: Familial C-Translokation: 46,XY.(2p–;Cp+)


Lurie