

## Noronet update, September 2012

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The major aim of Noronet is to share epidemiological and molecular data of norovirus outbreaks in order to detect trends and identify possible (foodborne) outbreaks. All data with submission data after December 31<sup>st</sup> 2009 and before August 8<sup>th</sup> 2012 was used for this update. Results are shown based on sample date and the shown typing results are according to the norovirus typing tool (Kroneman, Vennema et al. 2011).

### ***Outbreak reporting***

From January 1<sup>st</sup> 2012 until August 8<sup>th</sup> 2012, 876 outbreaks were submitted (by 10 countries), of which 2 outbreaks with a sampling date in 2008, 94 in 2009, 78 in 2010, 313 in 2011 and 389 in 2012. Outbreaks with a sampling date in 2012 were submitted by 6 countries (Finland, France, Germany, Hungary, The Netherlands and Sweden). China, Denmark, Japan and Spain have submitted outbreaks in 2012, but with a sampling year before 2012. In **table 1** the number of submitted outbreaks per country is shown based on sampling year. In 2012, 6 of 389 (2%) outbreaks were reported as mixed infections with adenovirus, rotavirus, astrovirus or aichi virus. Each outbreak report contains one or more norovirus sequences. For 2012 (based on sampling date) 31 NoV GI sequences were reported, 78 GII non II.4 sequences and 360 GII.4 sequences.

*Table 1 Number of norovirus outbreaks with sample date from January 1<sup>st</sup> 2010 until August 8<sup>th</sup> 2012 per country*

	2010	2011	2012	Total
AUSTRIA	54	21		<b>75</b>
BELGIUM	14	6		<b>20</b>
CHINA		77		<b>77</b>
DENMARK	11	23		<b>34</b>
FINLAND	283	94	45	<b>422</b>
FRANCE	215	204	108	<b>527</b>
GERMANY	50	62	1	<b>113</b>
HUNGARY	91	83	31	<b>205</b>
IRELAND	7			<b>7</b>
ITALY	1			<b>1</b>
JAPAN	41	24		<b>65</b>
NETHERLANDS	520	337	195	<b>1052</b>
SPAIN	41	4		<b>45</b>
SWEDEN	24	64	9	<b>97</b>
UNITED KINGDOM	9	6		<b>15</b>
<b>Total</b>	<b>1361</b>	<b>1005</b>	<b>389</b>	<b>2755</b>

## ***Genogroup I diversity and trends***

**Table 2** shows the genogroup I diversity of submitted sequences from January 1<sup>st</sup> 2010 until August 8<sup>th</sup> 2012 (n =231). Genotypes I.4, I.7 and I.b are the most frequently reported GI strains. In 2012 no striking changes were observed compared to the previous update. In order to identify international outbreak clusters, we searched for the presence of identical sequences between countries with sampling date from January 1<sup>st</sup> 2012 until August 8<sup>th</sup> 2012. In this period, no identical GI sequences between countries were found.

## ***Genogroup II non GII.4 diversity and trends***

In the shown period 605 genogroup II non GII.4 sequences were submitted (Table 3). In 2012 a total of 24 outbreaks were related to GII.g (ORF1) or GII.1 (ORF2) with 12 (50%) transmission route person to person, 5 (21%) food borne and 7 (29%) unknown. Of the 5 GII.g or GII.1 food borne related outbreaks, 2 (40%) were related to shellfish of which one was reported with a co-infection with Aichi virus. GII.g remained the dominant strain in 2012 and was reported by The Netherlands, Hungary, Finland and France. In 2012 the balance between the GII.g associated ORF2 strains, GII.1 and GII.12, remained in favor of GII.1. We identified one small cluster with three identical GII.7 sequences (figure 1) from two countries: France and Finland. Reported suspected transmission routes were unknown and person to person. One GII.7 sample from France and one from Finland had an onset of illness within two weeks from each other, so possibly these sequences are related.

*Table 2. Norovirus genogroup I sequence diversity from January 1<sup>st</sup> 2010 until August 8<sup>th</sup> 2012 grouped by sampling date*

	2010		2011		2012		Total	% of GG
	ORF1	ORF2	ORF1	ORF2	ORF1	ORF2		
I.1	1	4	2	3			10	4
I.2	3	2	3	1			9	4
I.3	4	5	7	7	4	3	30	13
I.4	26	17	19	16	3	5	86	37
I.5		1					1	0
I.6		7		11		3	21	9
I.7	17	7	3	2	5		34	15
I.a			1				1	0
I.b	9		22		5		36	16
I.f					3		3	1
<b>Total</b>	<b>60</b>	<b>43</b>	<b>57</b>	<b>40</b>	<b>20</b>	<b>11</b>	<b>231</b>	<b>100</b>

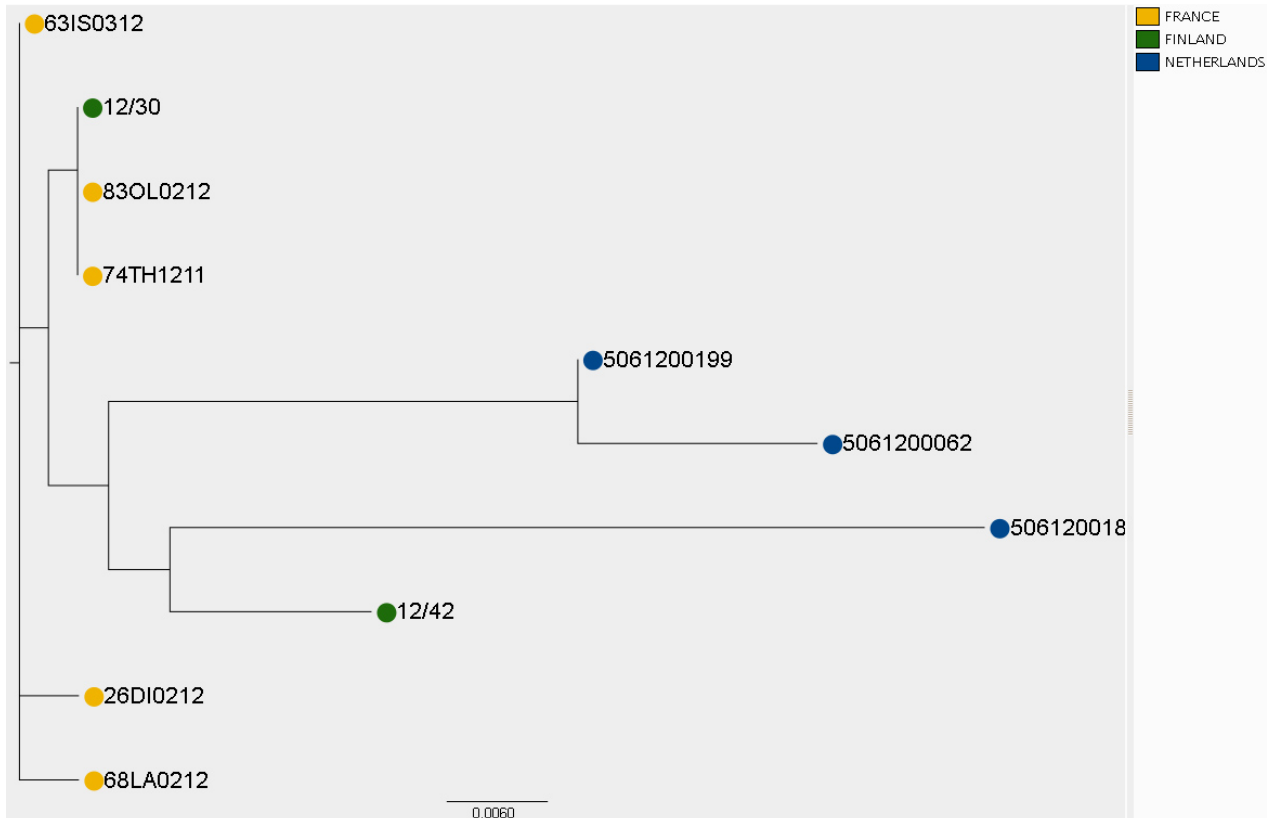


Figure 1 Neighbour-Joining tree (2-parameter Kimura nucleotide substitution model) of GII.7 sequences (minimum sequence overlap 195 nt) with sampling date from January 1<sup>st</sup> 2012 until August 8<sup>th</sup> 2012.

### GII.4 diversity and trends

In the shown period 2573 GII.4 sequences were submitted (Table 4). In 2012 GII.4 2010 remained the dominant variant and GII.4 2006b was reported occasionally. In the Noronet update of April 2012 a possible new GII.4 variant was mentioned which might have evolved from the GII.4 2010 variant. The previous analysis was repeated with addition of recently submitted GII.4 2010 sequences and GII.4 unassigned sequences (**figure 2 A -B and 3 AB**).

Figure 2A (ORF1, region A) and B (ORF2, region C) show the same clustering as in the previous update. Between the oldest and the most recent main clusters, there are 4-5 nucleotide changes in region A and region C, both approximately 250-300 nt in length. As stated in the previous update, these strains have remarkable sequence changes in region A and C. The most remarkable change in region A is a transversion from T to G in position 4516 relative to the Farmington Hills strain. Although this change does not result in an amino acid change, transversions are much more rare than transitions and are less likely to revert. A remarkable change in region C does result in an amino acid change; N54S. This change is rarely seen among all norovirus GII.4 strains, but present in 58% of recent strains. In 2012 the possible new strain is reported by four countries across Europe: Finland, France, Hungary and The Netherlands.

Figures 3A and B show the GII.4 unassigned variants (magenta) and GII.4 variant 2010 (blue), to identify unassigned clusters. An increase in the number of sequences which can not be assigned by the typing tool could be an indication of an emerging new cluster. In that case the unassigned sequences should cluster together in a phylogenetic tree. For both ORF1 region A and ORF2 region C such clustering is not apparent for recent strains.

In an e-mail to the NoroNet e-mail network of 3-8-2012, Peter White from Australia reported an emerging new GII.4 variant in Australia. He has submitted the sequences to the NoroNet database. We have included the ORF2 part of this sequence in the trees in Figure 2B and 3B. It clusters with two

sequences, submitted by Sweden and France with respective sample dates of January 2012 and December 2011. All three remained unassigned in the variant typing part of the typing tool.

*Table 3 Norovirus genogroup II non GII.4 sequence diversity from January 1<sup>st</sup> 2010 until August 8<sup>th</sup> 2012 grouped by sampling date*

	2010		2011		2012		Total	% of GG
	ORF1	ORF2	ORF1	ORF2	ORF1	ORF2		
II.1		31		17		6	<b>54</b>	<b>9</b>
II.2	14	3	6	10	1	1	<b>35</b>	<b>6</b>
II.3		6		38		2	<b>46</b>	<b>8</b>
II.6		8	1	32		14	<b>55</b>	<b>9</b>
II.7	30	3	42	14	11	2	<b>102</b>	<b>17</b>
II.8	3	1					<b>4</b>	<b>1</b>
II.12		32		4	4		<b>40</b>	<b>7</b>
II.13		13		4		1	<b>18</b>	<b>3</b>
II.14		1		1			<b>2</b>	<b>0</b>
II.15	1						<b>1</b>	<b>0</b>
II.16			3				<b>3</b>	<b>0</b>
II.21		2		1			<b>3</b>	<b>0</b>
II.b	33		18		13		<b>64</b>	<b>11</b>
II.e	5		4				<b>9</b>	<b>1</b>
II.g	86		52		23		<b>161</b>	<b>27</b>
NA	5	1	2		2		<b>8</b>	<b>1</b>
<b>Total</b>	<b>177</b>	<b>101</b>	<b>128</b>	<b>121</b>	<b>52</b>	<b>26</b>	<b>605</b>	<b>100</b>

*Table 4 Norovirus genogroup II.4 sequence diversity from January 1<sup>st</sup> 2010 until August 8<sup>th</sup> 2012 grouped by sampling date*

	2010		2011		2012		Total
	ORF1	ORF2	ORF1	ORF2	ORF1	ORF2	
II.4 2006a	1	1					<b>2</b>
II.4 2006b	108	33	16	48	11		<b>216</b>
II.4 2007		1		1			<b>2</b>
II.4 2008	28	1	2	2			<b>33</b>
II.4 2010	830	201	567	204	254	58	<b>2114</b>
II.4 NA	28	47	20	74	19	18	<b>206</b>
<b>II.4 total</b>	<b>995</b>	<b>284</b>	<b>605</b>	<b>329</b>	<b>284</b>	<b>76</b>	<b>2573</b>

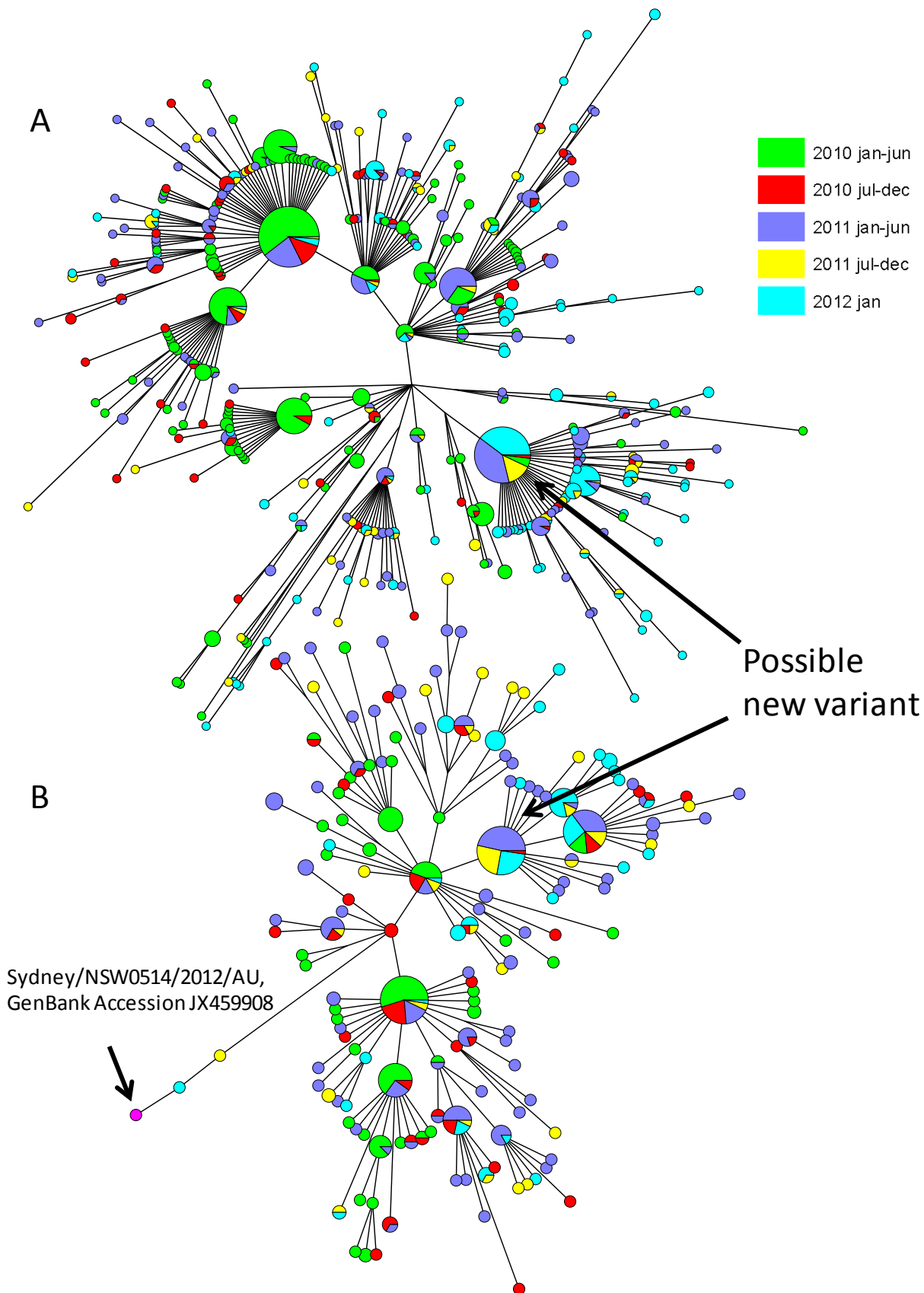


Figure 2 A and B: Norovirus GII.4 ORF1 region A, 1528 sequences GII.4 2010 and unassigned length 283 nt categorized on sampling date between 2010 – 2012 (A) and norovirus GII.4 ORF2 region C, 421 GII.4 2010 and unassigned sequences with length 218 nt categorized on sampling date between 2010 – 2012 (B).

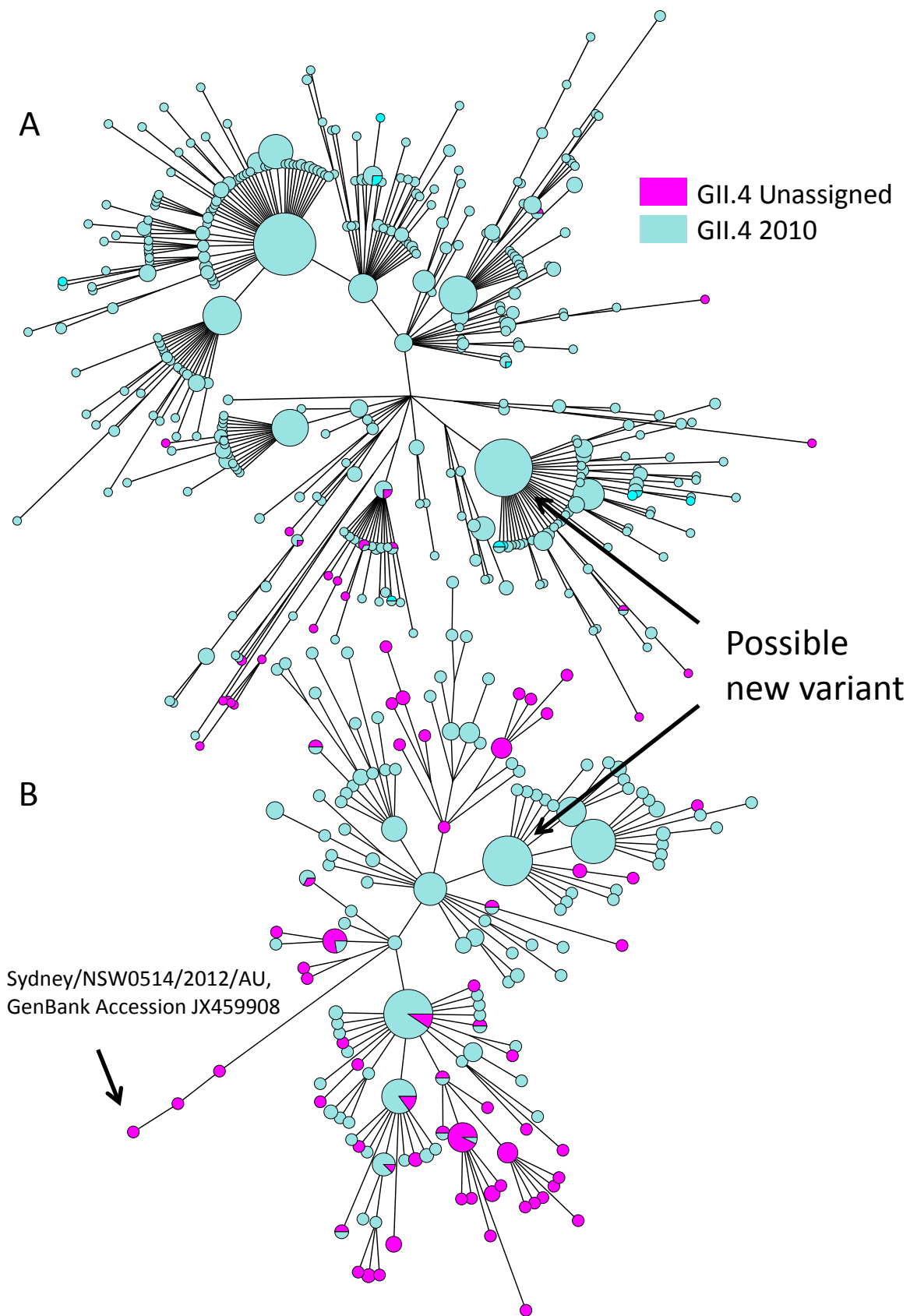


Figure 3 A and B Same trees as figure 2 a and b, colored by variant assignment

**References**

Kroneman, A., H. Vennema, et al. (2011). "An automated genotyping tool for enteroviruses and noroviruses." J Clin Virol **51**(2): 121-125.