AOE Analysis of AANP's Fall 2021 Membership Survey

A survey was sent to the membership base of the American Association of Neuropathologists (AANP) in the fall of 2021. This survey is used for planning of future annual meeting topics by providing a better understanding of current neuropathology practice characteristics. A total of 112 members provided responses to the 26 clinical assertion statement questions within the survey and the summary of these results are described below.

The survey asked individuals to provide responses to demographic questions, shown in figures 1-3, to help further contextualize the results.

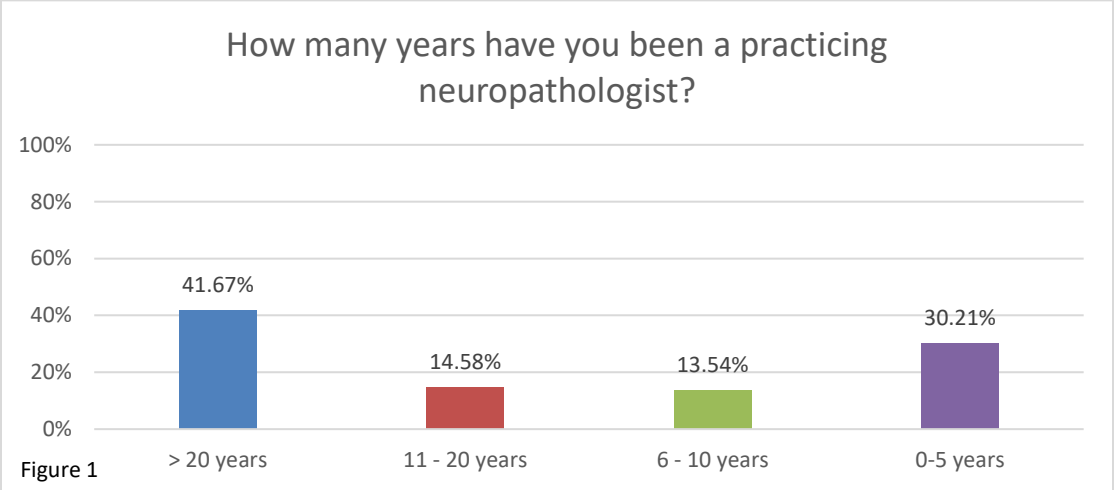

Figure 1

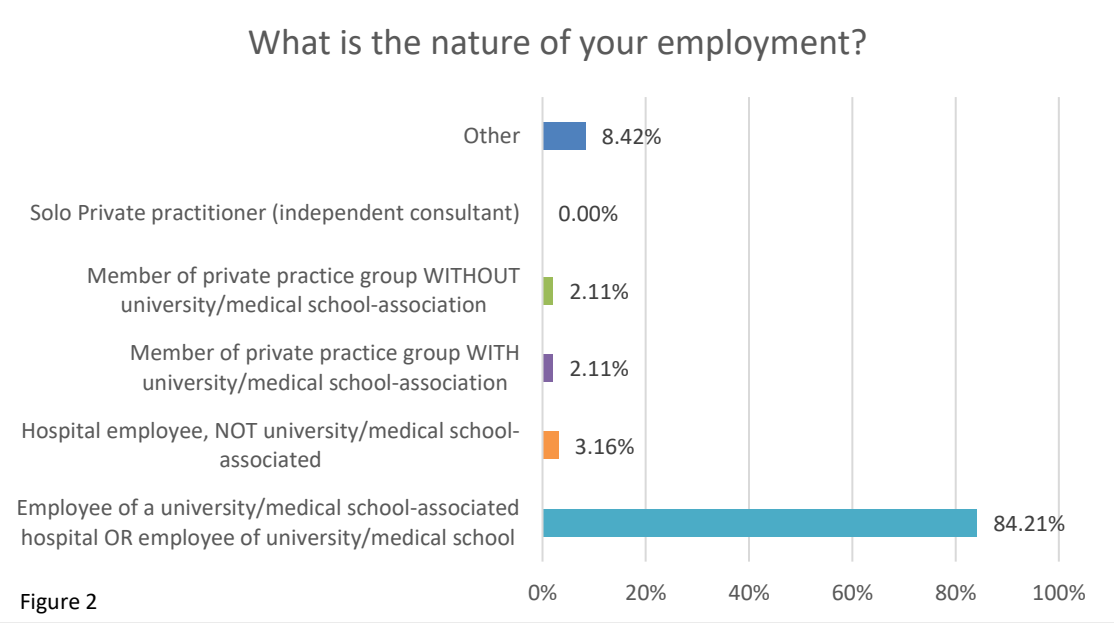

Figure 2

Other includes: Retired/Semi-Retired (2), Medical Student (1), Fellow/Forensic Fellow (2), Research Physician (1), Medical Examiner (1), Nonclinical hospital, active senior academic MD (1)

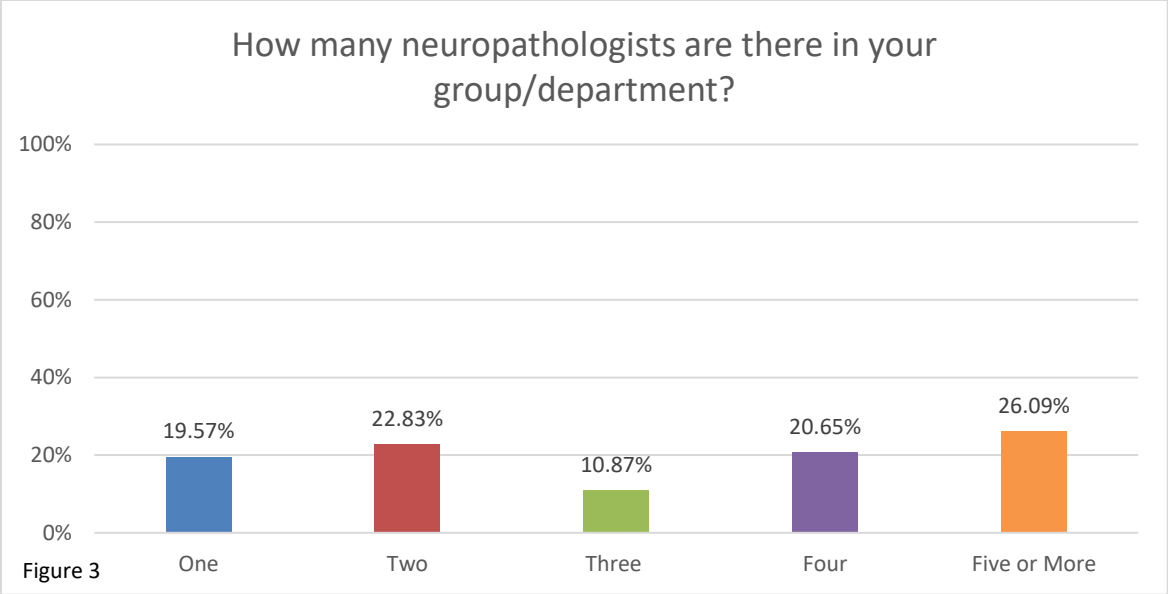

Figure 3

Clinical Assertion Statements

The survey asked members to rate 26 different clinical assertion statements using a 5-point Likert-type scale from 1=Disagree Completely to 5=Agree Completely, with a neutral option of 3=Neither Disagree nor Agree. These questions were developed to determine a member's level of knowledge regarding 9 separate topics in neuropathology. Data is presented as mean +/- standard deviation. Percentages indicate the number of responses in the incorrect/neutral position of total responses.

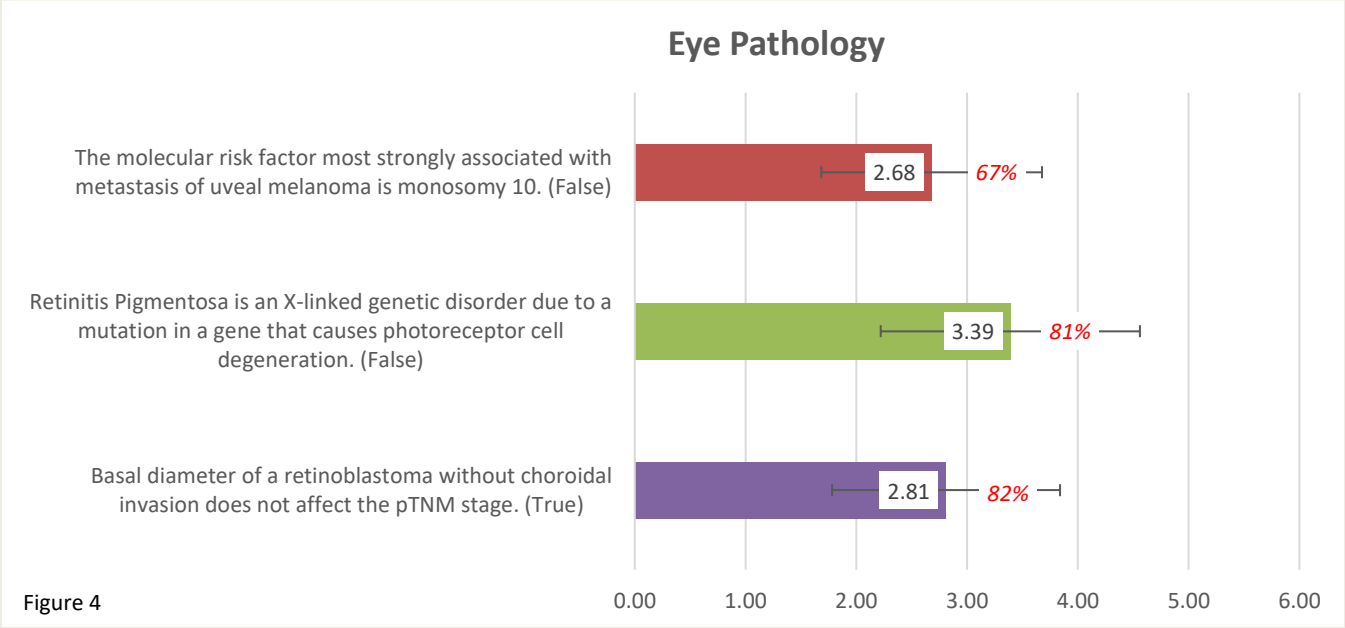

Figure 4

Figure 4 provides the results for the three questions evaluating knowledge in the area of **eye pathology**. Statements one and two are false, while statement three is true. Statement one had a mean score in the desired direction. However, statement one had 67% of the respondents who answered at the neutral/incorrect position

which may indicate where additional education is appropriate. Statements two and three had mean scores in the incorrect direction. In sum, areas of appropriate additional education include:

- The molecular risk factor most strongly associated with metastasis of uveal melanoma is monosomy 10. (False)
- Retinitis Pigmentosa is an X-linked genetic disorder due to a mutation in a gene that causes photoreceptor cell degeneration. (False)
- Basal diameter of a retinoblastoma without choroidal invasion does not affect the pTNM stage. (True)

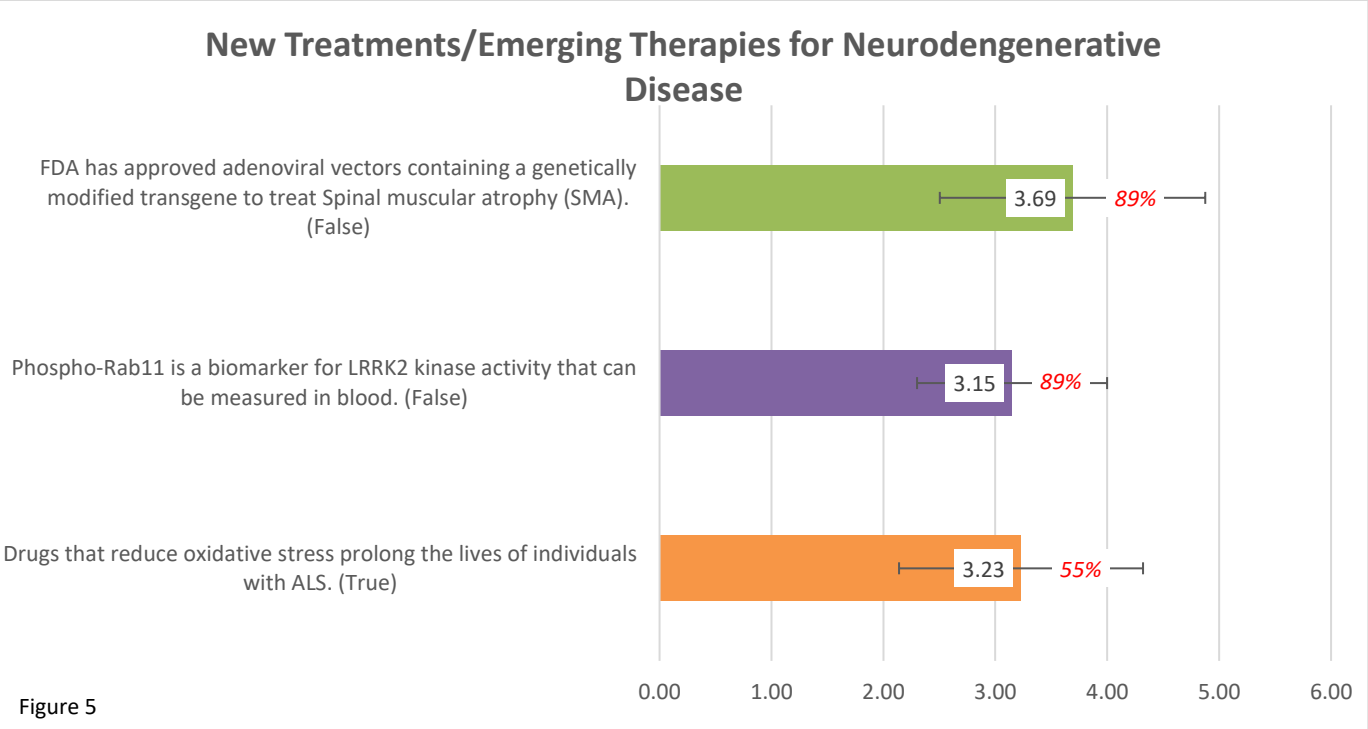

Figure 5

Figure 5 provides the results for the three questions evaluating knowledge in the area of **new treatments and emerging therapies for neurodegenerative disease.** Statements one and two are false, while statement three is true. Statement one had a mean score on the incorrect side of the scale indicating that additional education is appropriate. Statements two and three had mean scores in neutral position, with 89% and 55% of responses, respectively, in the incorrect or neutral, indicating additional education is needed. In sum, areas of appropriate additional education include:

- FDA has approved adenoviral vectors containing a genetically modified transgene to treat Spinal muscular atrophy (SMA). (False)
- Phospho-Rab11 is a biomarker for LRRK2 kinase activity that can be measured in blood. (False)
- Drugs that reduce oxidative stress prolong the lives of individuals with ALS. (True)

Figure 6

Figure 6 provides the results for the three questions evaluating knowledge in the area of **ethics.** Statement one is true, while statements two and three are false. Statement one and two have a mean close to the neutral position, additionally, 55% responses were incorrect or in the neutral position, for each, indicating education is appropriate related to these statements. Statement three had a mean score in the incorrect direction. In sum, areas of appropriate additional education include:

- Case reports and small case series do not meet criteria for research or require IRB approval based on Federal Regulations. (True)
- IRB approval is required for autopsy cohort studies.(False)
- Artificial intelligence research methods on deidentified clinical laboratory data have been determined to pose little risk to patient safety. (False)

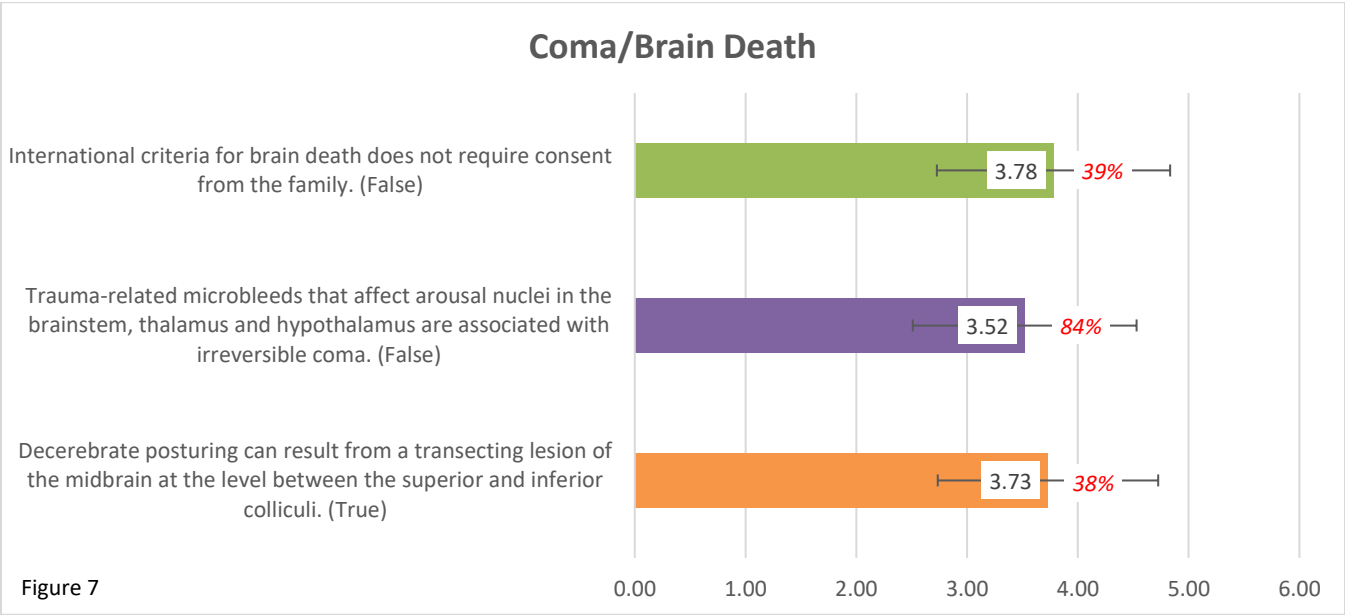

Figure 7

Figure 7 provides the results for the three questions evaluating knowledge in the area of **coma/brain death**. Statements one and two are false, while statement three is true. Members selected responses in the desired direction for statement three. Statements one and two had a mean score on the incorrect side of the scale indicating additional education is appropriate:

- International criteria for brain death does not require consent from the family. (False)
- Trauma-related microbleeds that affect arousal nuclei in the brainstem, thalamus and hypothalamus are associated with irreversible coma. (False)

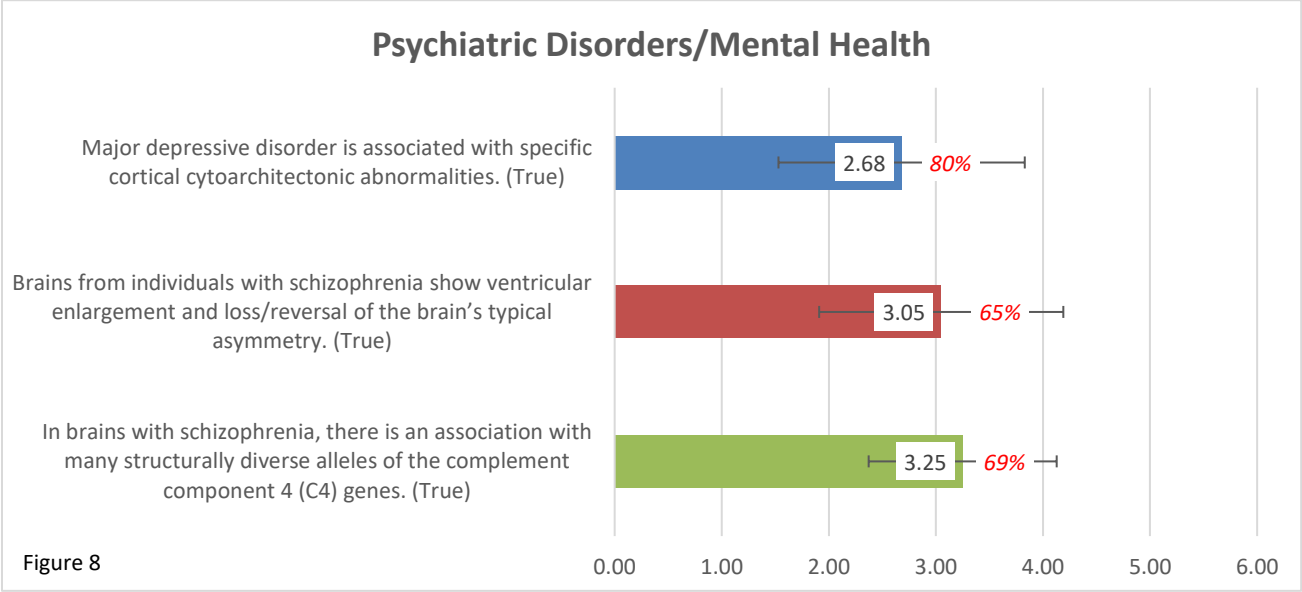

Figure 8

Figure 8 provides the results for the three questions evaluating knowledge in the area of **psychiatric disorders and mental health**. All three statements are true. Statement three had a mean score in the desired direction, however 69% of responses were incorrect or neutral. Additionally, statements one and two had answers in the incorrect or neutral position, indicating that education may be appropriate. In sum, areas of appropriate additional education include:

- Major depressive disorder is associated with specific cortical cytoarchitectonic abnormalities. (True)
- Brains from individuals with schizophrenia show ventricular enlargement and loss/reversal of the brain's typical asymmetry. (True)
- In brains with schizophrenia, there is an association with many structurally diverse alleles of the complement component 4 (C4) genes. (True)

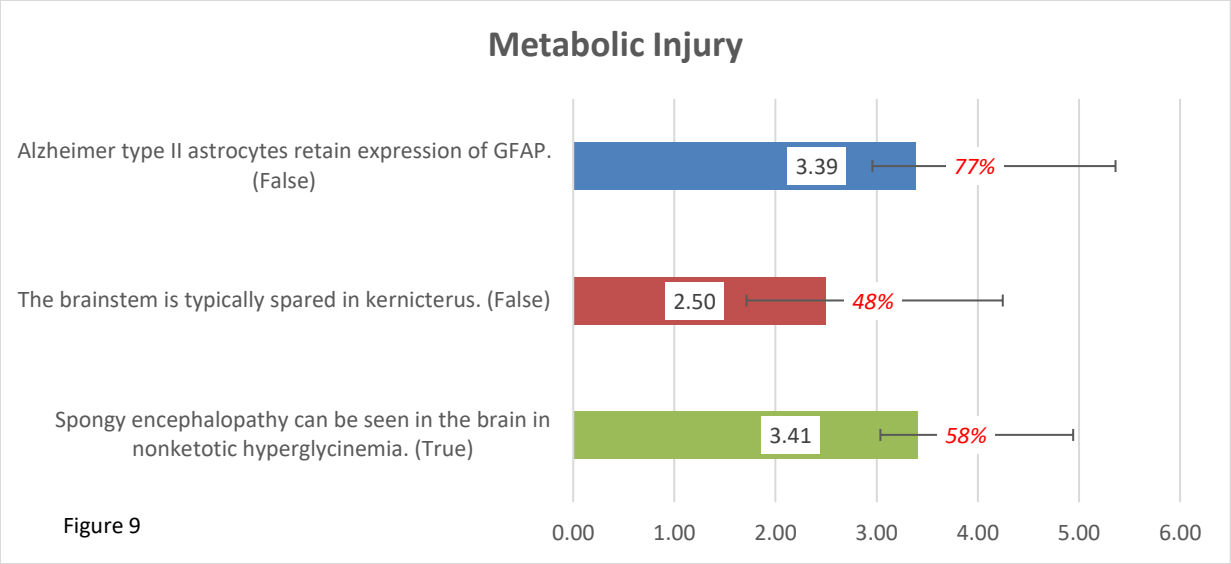

Figure 9

Figure 9 provides the results for the three questions evaluating knowledge in the area of **metabolic injury**. Statement one and two is false and statement three is true. Statements two and three had mean scores in the correct direction. Statement one had a mean score in the incorrect direction, with 77% of respondents answering in the neutral or incorrect direction. In sum, an area of appropriate additional education include:

- Alzheimer type II astrocytes retain expression of GFAP. (False)

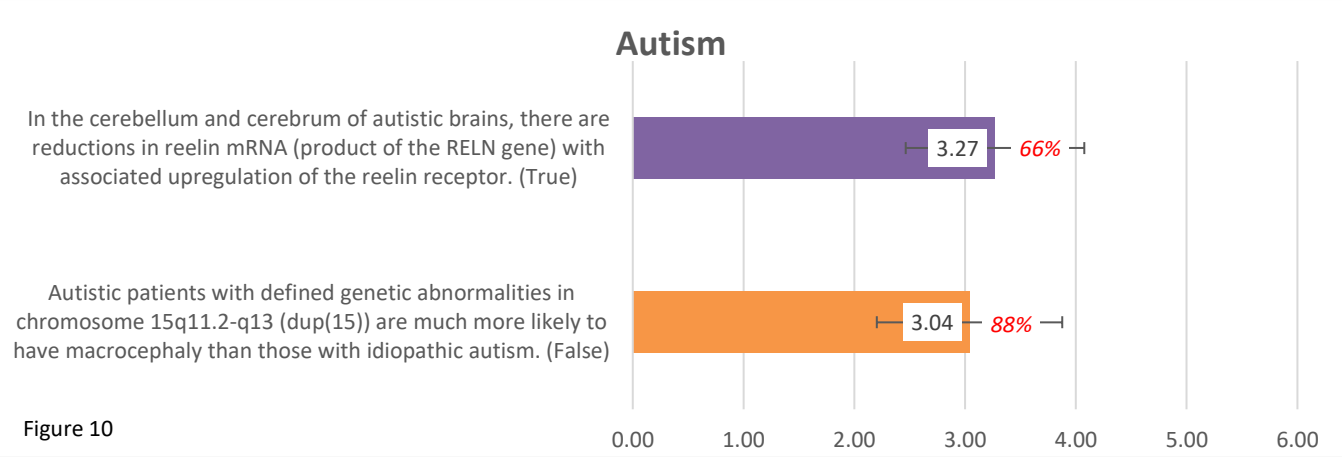

Figure 10

Figure 10 provides the results for the two questions evaluating knowledge in the areas of **autism**. Statement one is false, while statement two is true. Statement one had a mean score in the incorrect direction, additionally 66% of respondents answered in the incorrect or neutral position. Statement two had a mean score in the neutral position, with 88% of respondents answering in the incorrect or neutral position, indicating education is appropriate. In sum, areas of appropriate additional education include:

- Autistic patients with defined genetic abnormalities in chromosome 15q11.2-q13 (dup(15)) are much more likely to have macrocephaly than those with idiopathic autism. (False)
- In the cerebellum and cerebrum of autistic brains, there are reductions in reelin mRNA (product of the RELN gene) with associated upregulation of the reelin receptor. (True)

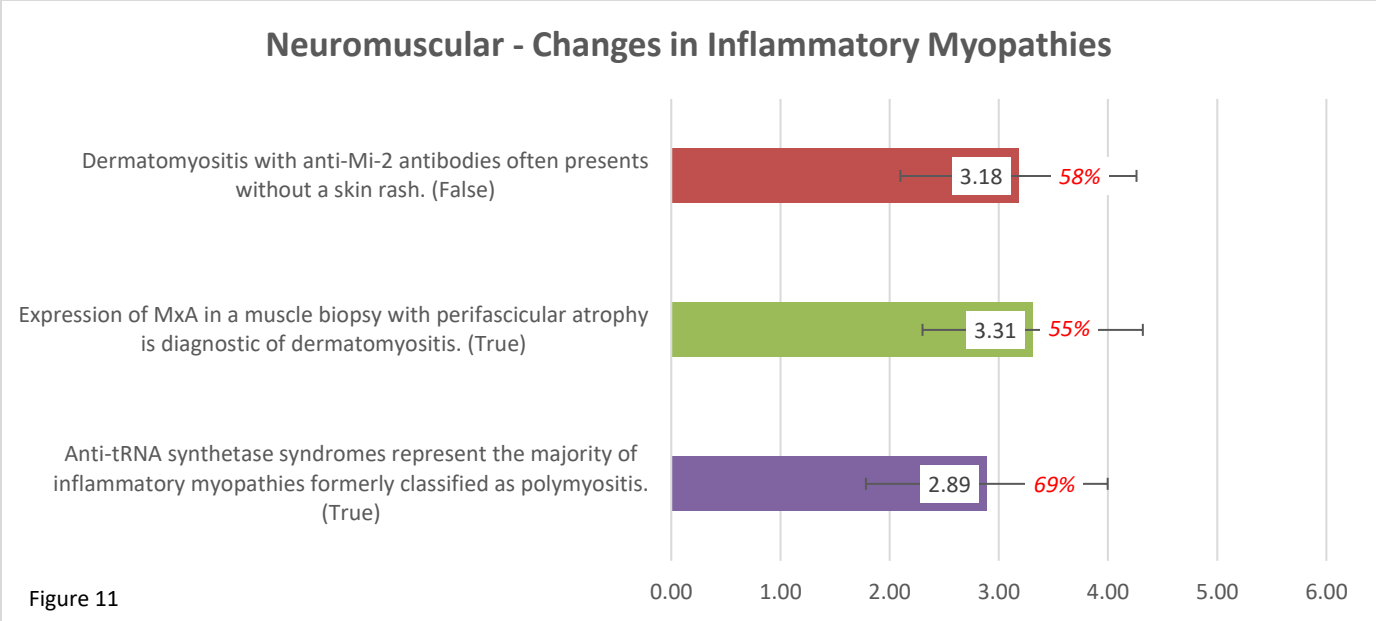

Figure 11

Figure 11 provides the results for the three questions evaluating knowledge in the area of **neuromuscular – changes in inflammatory myopathies**. Statement one is false, while statements two and three are true. Statement two has a mean score in the desired direction, while statements one and three are on the incorrect side. In sum, areas of appropriate additional education include:

- Dermatomyositis with anti-Mi-2 antibodies often presents without a skin rash. (False)
- Anti-tRNA synthetase syndromes represent the majority of inflammatory myopathies formerly classified as polymyositis. (True)

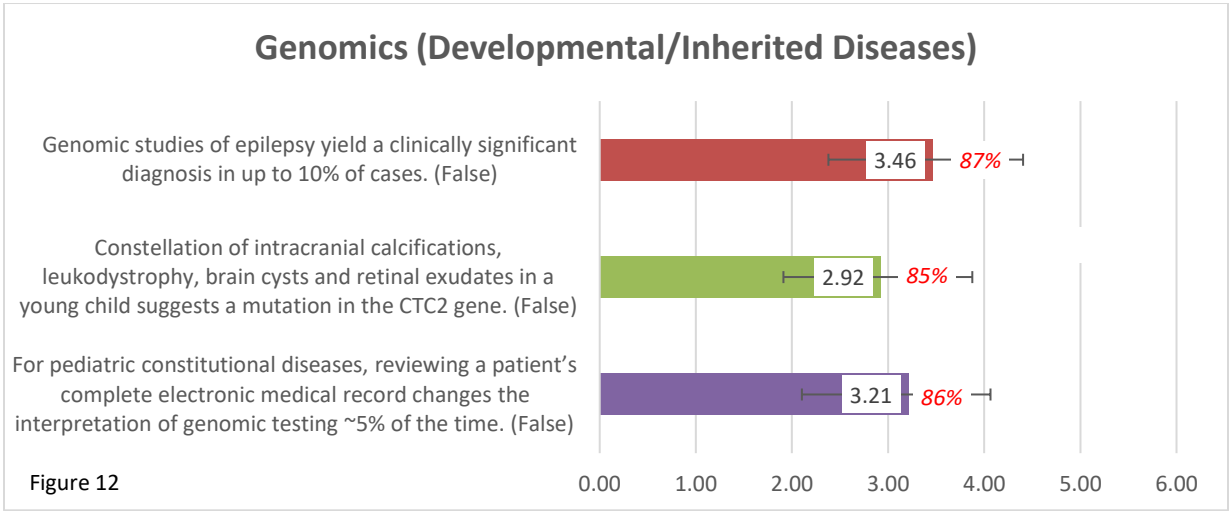

Figure 12

Figure 12 provides the results for the three questions evaluating knowledge in the area of **genomics (developmental/inherited diseases)**. All three statements are false. Statement two had a mean score in the desired direction, however, 85% of respondents answered incorrectly or in the neutral position, indicating more

education may be appropriate. Statements one and three had mean scores on the incorrect side. In sum, areas of appropriate additional education include:

- Genomic studies of epilepsy yield a clinically significant diagnosis in up to 10% of cases. (False)
- Constellation of intracranial calcifications, leukodystrophy, brain cysts and retinal exudates in a young child suggests a mutation in the CTC2 gene. (False)
- For pediatric constitutional diseases, reviewing a patient's complete electronic medical record changes the interpretation of genomic testing ~5% of the time. (False)

Conclusion:

Based on the analysis of the 2021 Membership Survey, there were some statements where responses were close to neutral and many respondents answered in the neutral position which provides areas where there may be need for additional education. Further, several scores were on the opposite/wrong side of the scale. Both situations indicate that the following are areas of need for additional education:

- **Eye Pathology**
  - The molecular risk factor most strongly associated with metastasis of uveal melanoma is monosomy 10. (False statement, 67% unknown/incorrect responses)
  - Retinitis Pigmentosa is an X-linked genetic disorder due to a mutation in a gene that causes photoreceptor cell degeneration. (False statement, 80% unknown/incorrect responses)
  - Basal diameter of a retinoblastoma without choroidal invasion does not affect the pTNM stage. (True statement, 82% unknown/incorrect responses)
- **New Treatments/Emerging Therapies for Neurodegenerative Disease**
  - FDA has approved adenoviral vectors containing a genetically modified transgene to treat Spinal muscular atrophy (SMA). (False statement, 89% unknown/incorrect responses)
  - Phospho-Rab11 is a biomarker for LRRK2 kinase activity that can be measured in blood. (False statement, 89% unknown/incorrect responses)
  - Drugs that reduce oxidative stress prolong the lives of individuals with ALS. (True statement, 55% unknown/incorrect responses)
- **Ethics**
  - Case reports and small case series do not meet criteria for research or require IRB approval based on Federal Regulations. (True statement, 55% unknown/incorrect responses)
  - IRB approval is required for autopsy cohort studies.(False statement, 55% unknown/incorrect responses)
  - Artificial intelligence research methods on deidentified clinical laboratory data have been determined to pose little risk to patient safety. (False statement, 85% unknown/incorrect responses)
- **Coma/Brain Death**
  - International criteria for brain death does not require consent from the family. (False statement, 39% unknown/incorrect responses)
  - Trauma-related microbleeds that affect arousal nuclei in the brainstem, thalamus and hypothalamus are associated with irreversible coma. (False statement, 84% unknown/incorrect responses)

- **Psychiatric Disorders/Mental Health**
  - Major depressive disorder is associated with specific cortical cytoarchitectonic abnormalities. (True statement, 80% unknown/incorrect responses)

    - Brains from individuals with schizophrenia show ventricular enlargement and loss/reversal of the brain's typical asymmetry. (True statement, 65% unknown/incorrect responses)
    - In brains with schizophrenia, there is an association with many structurally diverse alleles of the complement component 4 (C4) genes. (True statement, 69% unknown/incorrect responses)
- **Metabolic Injury**
    - Alzheimer type II astrocytes retain expression of GFAP. (False statement, 77% unknown/incorrect responses)
- **Autism**
    - Autistic patients with defined genetic abnormalities in chromosome 15q11.2-q13 (dup(15)) are much more likely to have macrocephaly than those with idiopathic autism. (False statement, 66% unknown/incorrect responses)
    - In the cerebellum and cerebrum of autistic brains, there are reductions in reelin mRNA (product of the RELN gene) with associated upregulation of the reelin receptor. (True statement, 88% unknown/incorrect responses)
- **Neuromuscular – Changes in Inflammatory Myopathies**
    - Anti-tRNA synthetase syndromes represent the majority of inflammatory myopathies formerly classified as polymyositis. (True statement, 69% unknown/incorrect responses)
    - Dermatomyositis with anti-Mi-2 antibodies often presents without a skin rash. (False statement, 58% unknown/incorrect responses)
- **Genomics (Developmental/Inherited Diseases)**
    - Genomic studies of epilepsy yield a clinically significant diagnosis in up to 10% of cases. (False statement, 87% unknown/incorrect responses)
    - Constellation of intracranial calcifications, leukodystrophy, brain cysts and retinal exudates in a young child suggests a mutation in the CTC2 gene. (False statement, 85% unknown/incorrect responses)
    - For pediatric constitutional diseases, reviewing a patient's complete electronic medical record changes the interpretation of genomic testing ~5% of the time. (False statement, 86% unknown/incorrect responses)

Additional Survey Questions

The following data regarding prion disease and molecular testing for glioma diagnosis was collected in order for the AANP to gather data that may help the organization achieve *Accreditation with Commendation* through the Accreditation Council for Continuing Medical Education (ACCME) during its next reaccreditation cycle.

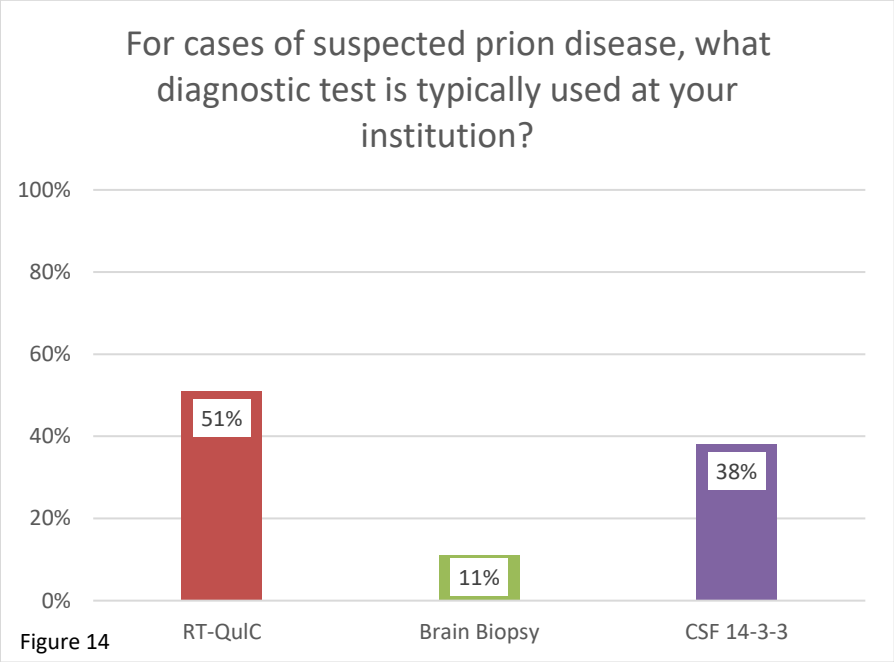

Figure 14

Figure 14 provides the results for the type of diagnostic tests used in cases of suspected prion disease at members' institutions. Most members, 51%, use Real-time quaking-induced conversion (RT-QulC) testing to determine the presence of prion disease.

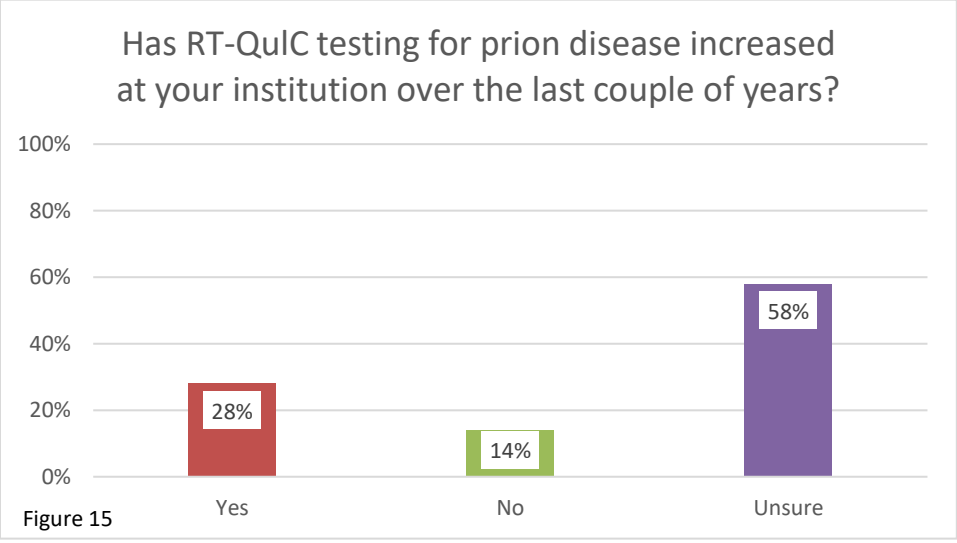

Figure 15

Figure 15 provides the results assessing the frequency of use of RT-QulC in members' institutions in recent years. Many members (58%) are unsure if there has been a change, while 28% do report an increased use of RT-QulC to test for suspected prion disease.

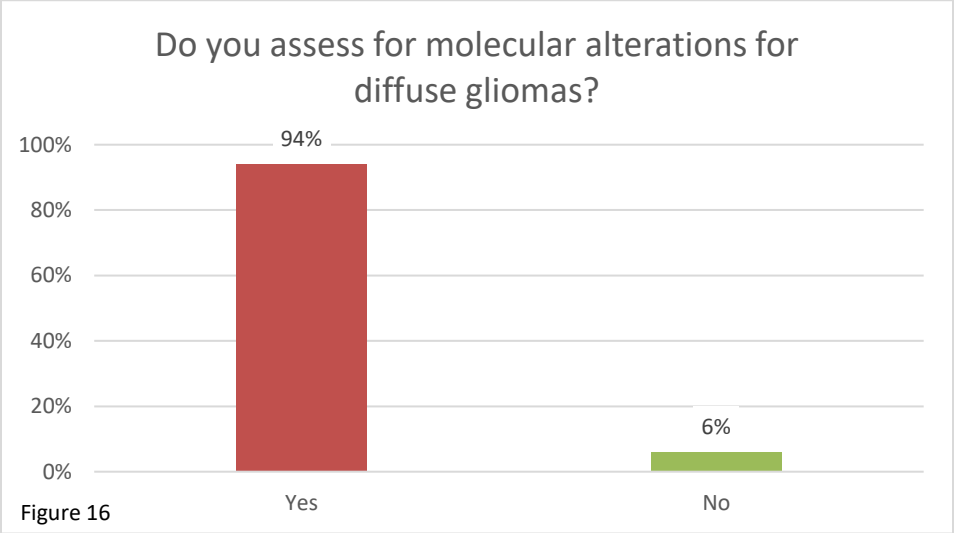

Figure 16

Figure 16 provides the results assessing the frequency of testing for molecular changes of diffuse gliomas at members' institutions. Testing can occur in-house or can be sent out to another lab. The overwhelming majority of members, 94%, indicated that this type of testing was used at their institution.

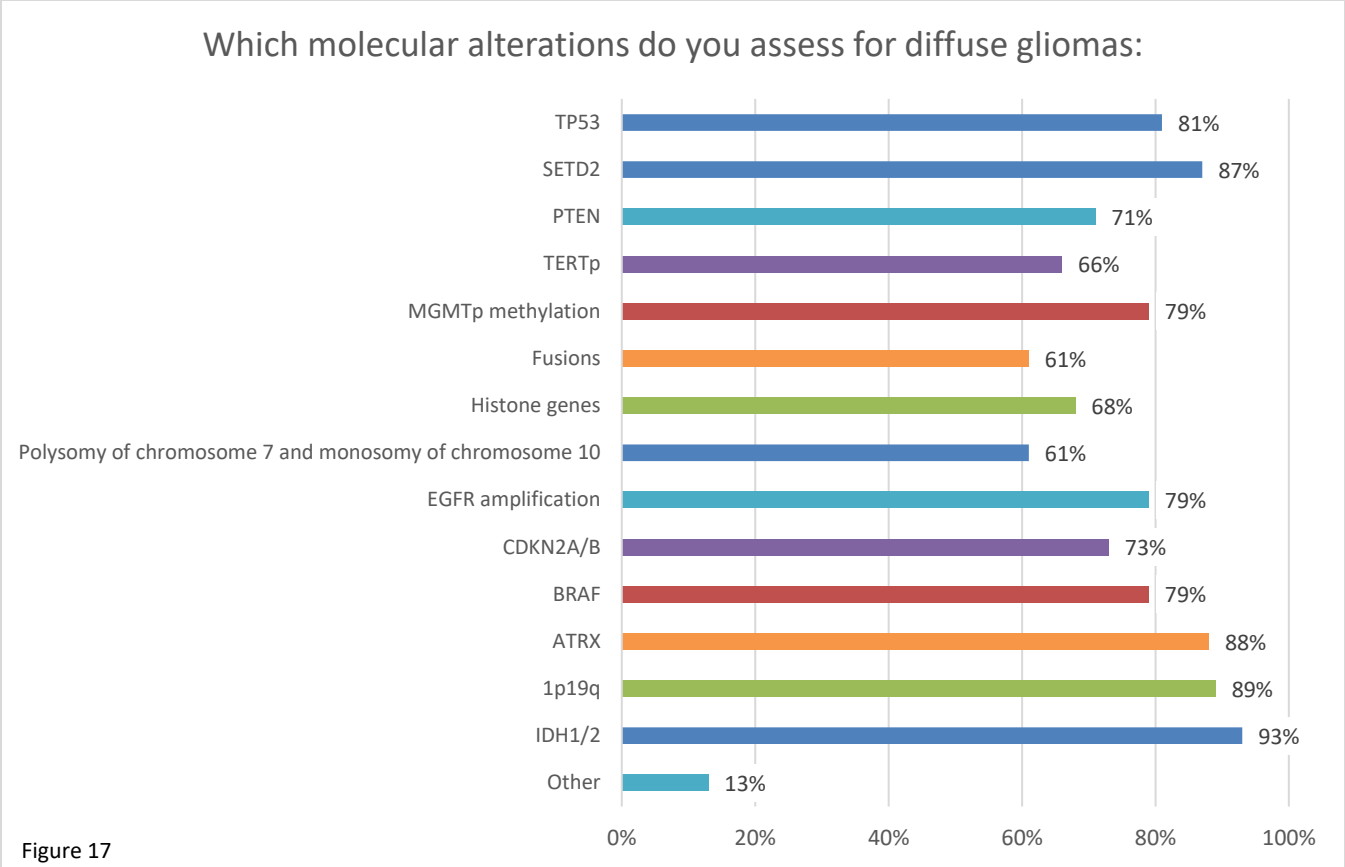

Figure 17

Figure 17 provides the results of which molecular markers members use to assess diffuse gliomas for molecular alterations. Testing can occur in-house or can be sent out to another lab. The most frequently used, with a response rate at >75% are: TP53, SETD2, MGMTp methylation, EGFR amplification, BRAF, ATRX, 1p19q and IDH1/2.

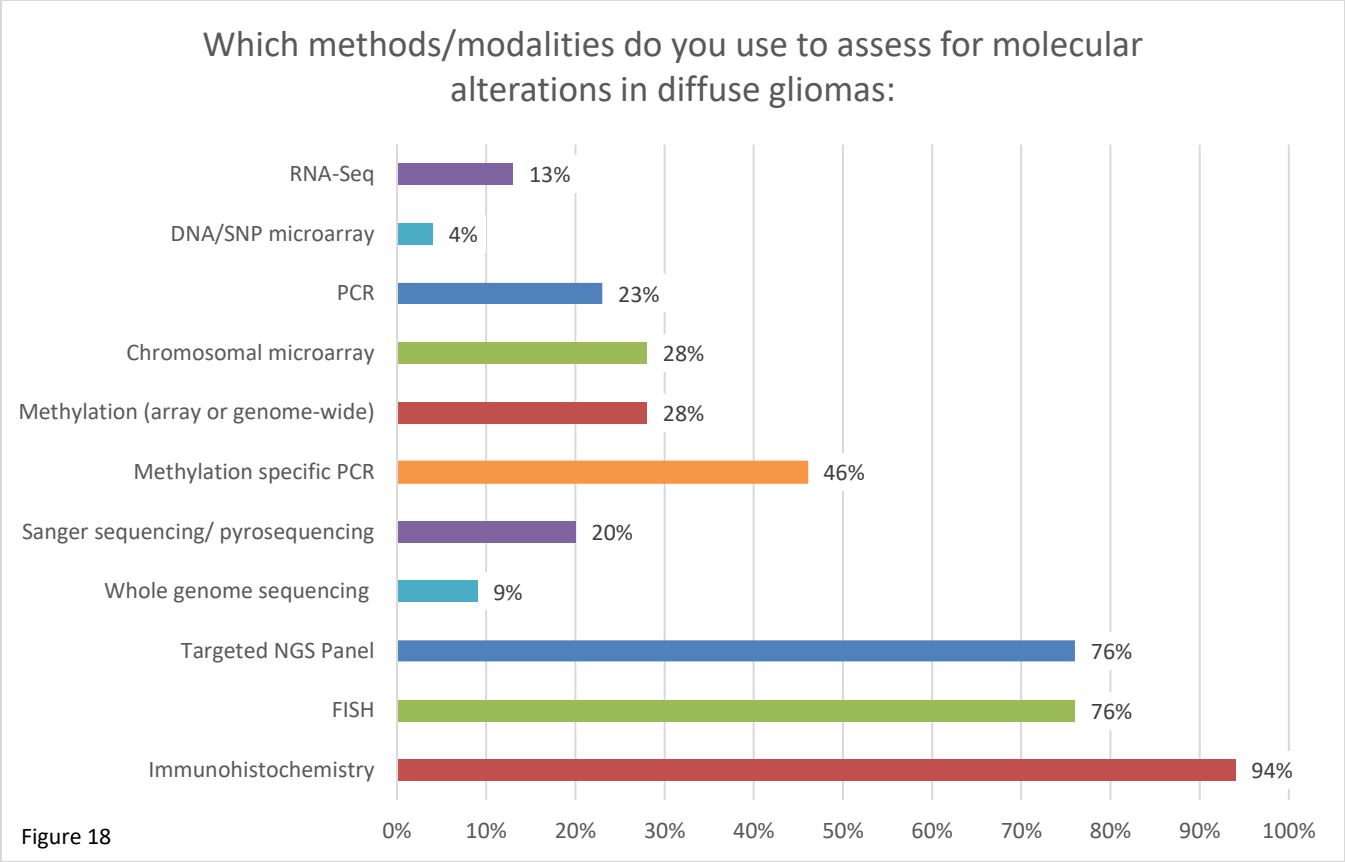

Figure 18

Figure 18 provides the results of type of testing members use to assess diffuse gliomas for molecular alterations. Testing can occur in-house or can be sent out to another lab. The most frequently used, with a response rate at >75% are: Targeted NGS panel, FISH and Immunohistochemistry.