Merlin Immunohistochemistry for Meningioma Diagnosis

Background

- **Merlin** is the tumor suppressor protein encoded by the **NF2 gene** on chromosome 22q.
- In **sporadic meningiomas**, especially of lateral or convexity location and higher grade, **NF2 deletions/mutations** are frequent.
- Loss of merlin expression has been proposed as a **surrogate immunohistochemical marker** for NF2 inactivation.

Immunohistochemistry Technique

- **Antibodies**: N-terminal, C-terminal, and **phosphorylated merlin (Ser518)**.
- **Tissue**: Formalin-fixed, paraffin-embedded meningioma samples.
- **Scoring**: Semi-quantitative (intensity and extent of cytoplasmic staining).

Findings from Tollefsen et al.

- Study of **172 meningiomas**, with 20 having known **NF2 status**.
- All tumors showed some level of **merlin immunoreactivity**, including phosphorylated merlin.
- **Phospho-merlin** was more expressed in **meningothelial subtypes**.
- No consistent correlation between **IHC merlin expression and NF2 mutation/deletion**.
- No clear association with **WHO grade** or **clinical outcome**

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⚖ Strengths and Limitations

Strengths

- Widely available and low-cost.
- Morphological correlation possible.
- Phospho-merlin gives insights into **functional status** of merlin.

Limitations

- **No strong correlation** with NF2 gene alterations.
- **Phosphorylated merlin** may be misleading (inactive form still stains).
- Variability in IHC interpretation and scoring.
- Risk of non-specific staining.

Clinical Implications

- **Merlin IHC is not a reliable surrogate marker** for NF2 mutation.
- Should not replace **molecular techniques** (NGS, FISH).
- Can be used as **supportive information** in context (e.g., NF2-related meningiomatosis).
- Most useful in **research** and subtype analysis.

Conclusion

Merlin immunohistochemistry offers biological insight into meningiomas but lacks the specificity and predictive value required for routine use as a surrogate for NF2 status. **Molecular confirmation is essential.**

References

1)
Tollefsen SE, Meta R, Solheim O, Mjønes P, Vestrheim I, Sjursen W, Torp SH. Merlin immunoreactivity fails to predict neurofibromatosis type 2 mutations in human meningiomas. J Neuropathol Exp Neurol. 2025 May 30:nlaf058. doi: 10.1093/jnen/nlaf058. Epub ahead of print. PMID: 40447281.