CAMM 535 Final Project — Report 1
Group 4: Schwannoma

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January 2026

Abstract

This report documents data acquisition and the conceptual database design for Schwannoma. We integrate multiple biological databases to construct a unified schema linking phenotype-related genes, variants, genomic coordinates, proteins, and GEO2R results.

Contents

1 Part 1 — Disease / Phenotype Introduction

Schwannoma is a typically benign, slow-growing peripheral nerve sheath tumor that arises from Schwann cells, the glial cells responsible for myelination of peripheral nerves. Schwannomas most commonly affect cranial and spinal nerves and are frequently associated with the vestibular branch of the eighth cranial nerve, where they are known as vestibular schwannomas (also called acoustic neuromas) [1].

1.1 Clinical characteristics

Clinically, schwannomas usually present as well-circumscribed, encapsulated tumors. Symptoms depend on tumor location and size and may include hearing loss, tinnitus, balance disturbances, localized pain, or neurological deficits due to nerve compression. Vestibular schwannomas represent the most common subtype and account for approximately 8–10% of all intracranial tumors [2]. Although most schwannomas are sporadic, bilateral vestibular schwannomas are a hallmark feature of neurofibromatosis type 2 (NF2), a hereditary tumor predisposition syndrome [3].

1.1.1 Annual incidence (sporadic vestibular schwannoma)

Population-based registry data suggest that sporadic vestibular schwannoma (VS) is diagnosed at an annual rate on the order of a few cases per 100,000 people. In a recent UK cohort registry study (2013–2016), the mean annual incidence of newly diagnosed VS was reported as **2.2 per 100,000 person-years**, with incidence rising strongly with age and peaking in the **60–69** year group (about **5.8 per 100,000 person-years**) [8]. Consistent with this scale, recent US population-based surveillance (CBTRUS, 2017–2021) reports an age-adjusted incidence rate for **vestibular schwannoma of 1.52 per 100,000** and shows that vestibular schwannoma constitutes the majority of non-malignant nerve sheath tumors in the CNS (Figure 1) [9].

1.2 Biological relevance

From a biological perspective, schwannomas provide an important model for studying tumor suppressor gene dysfunction and dysregulated cell signaling in glial-derived tumors. Schwann cells play a critical role in axonal support and nerve regeneration, and disruption of their growth control mechanisms can lead to uncontrolled proliferation. Schwannoma cells typically retain a benign histological appearance, yet they can cause significant morbidity due to their anatomical location and compressive growth pattern [4].

1.3 Known genetic associations

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The most well-established genetic association in schwannoma is loss-of-function mutation or deletion of the *NF2* gene, which encodes the tumor suppressor protein merlin (schwannomin). Merlin is a key regulator of contact inhibition and multiple signaling pathways, including Hippo, PI3K/AKT, and MAPK pathways [5]. In sporadic schwannomas, somatic alterations of *NF2*

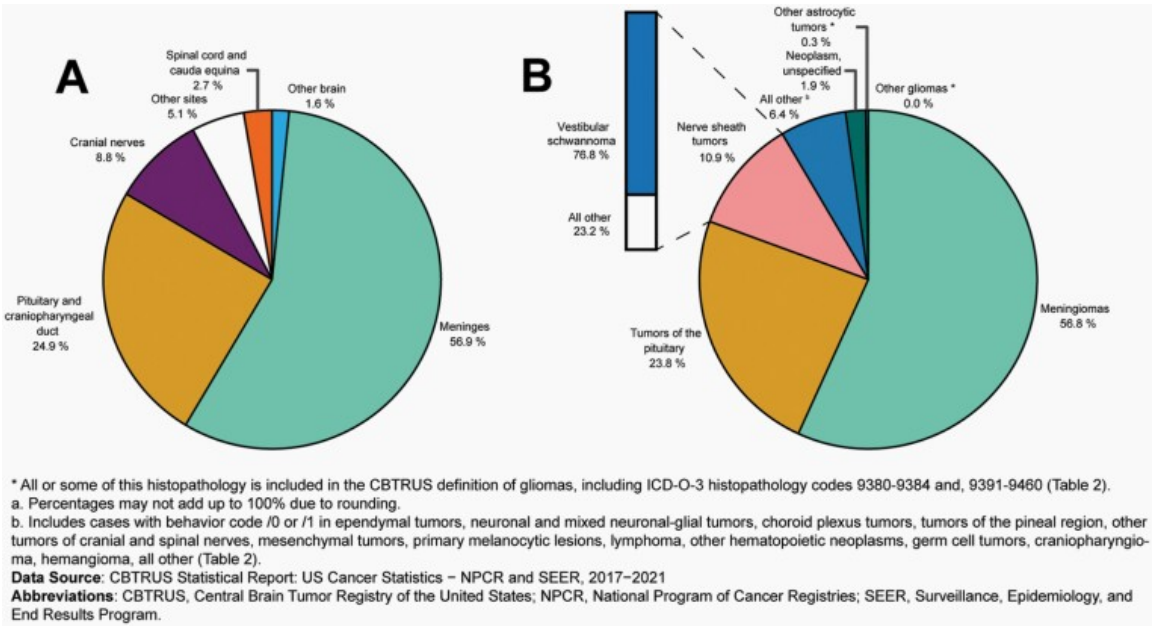

Figure 1. CBTRUS (US, 2017–2021): distribution of non-malignant primary brain/CNS tumors by (A) site and (B) histopathology. Panel B highlights that vestibular schwannoma represents a large fraction of nerve sheath tumors. Adapted from [9].

are observed in a majority of cases, while germline mutations are characteristic of patients with NF2-associated disease. Additional genetic and epigenetic alterations involving pathways related to cytoskeletal organization and cell adhesion have also been reported, highlighting the molecular heterogeneity of schwannomas [6].

As illustrated in Figure 2, disruption of merlin-mediated signaling removes critical growth-inhibitory signals in Schwann cells.

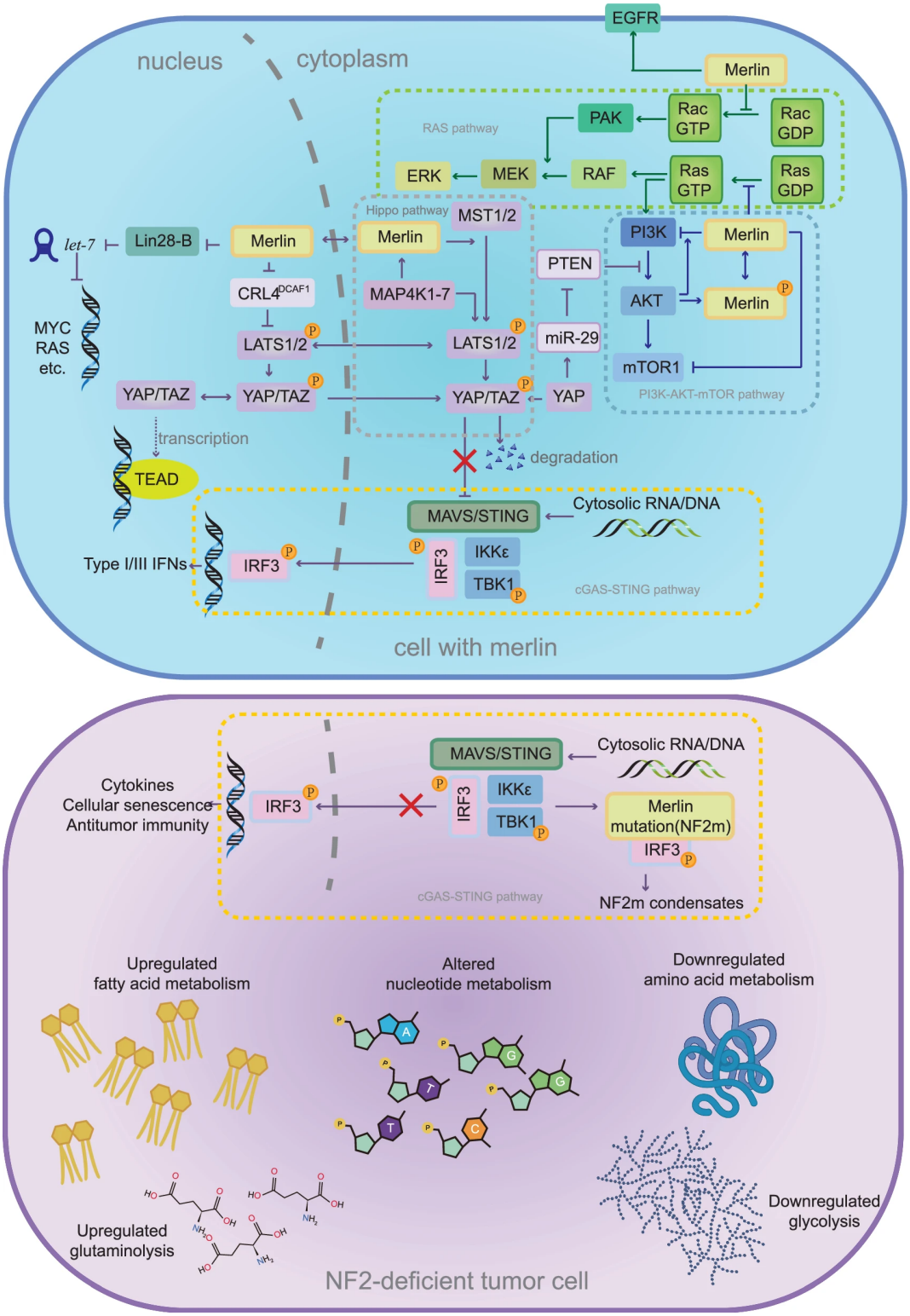

Figure 2. NF2/merlin signaling pathways in schwannoma development. Merlin regulates multiple growth-control pathways, including Hippo, PI3K/AKT, and MAPK signaling. Loss of NF2 function removes growth inhibition in Schwann cells and promotes tumor formation. Adapted from [7].

2 Part 2 — BioMart → STRING → Variants

2.1 Gene list retrieval from BioMart

Tool: **Ensembl BioMart**.

- Dataset: *Homo sapiens genes (GRCh38.pXX).*
- Filters: phenotype/disease term (Schwannoma) or equivalent.
- Attributes exported: gene symbol, Ensembl Gene ID, (optional) RefSeq ID, chr, start/end.

2.2 Network expansion using STRING

Tool: **STRING** (Human).

- Input: BioMart gene symbols (multiple input).
- Expansion: first shell, maximum 100 interactors.

2.3 Variant retrieval and mapping

Tool: **Ensembl BioMart** (variants/dbSNP). Explain how you ensured each variant maps to a gene in the expanded network, and list any ambiguities.

3 Part 3 — UCSC Table Browser (RefSeq coordinates)

Describe UCSC settings and outputs (genome build, table, attributes).

4 Part 4 — UniProt ID Mapping (Genes → Proteins)

Describe UniProt mapping settings and downloaded attributes (UniProt IDs, length, PDB, mass, function, location, etc.).

5 Part 5 — GEO Dataset & GEO2R

Describe GEO search constraints (human, since Jan 1 2005), chosen dataset, and the GEO2R output table.

6 Part 6 — Additional Table from Another Database

Add at least one additional table and explain how it links (or add a cross-reference table).

7 Part 7 — Conceptual Design (ER Diagram + Keys)

7.1 Entity-Relationship diagram

7.2 Primary keys and foreign keys

List PK/FK per table (you can use bullets or a small table).

8 Challenges and Ambiguities

Summarize issues (ID mismatches, missing mappings, non-coding genes, isoforms, etc.).

References

References

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