

Tenosynovial Giant Cell Tumor

Localized and diffuse types: pathogenesis, morphology, clinical patterns

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Learning objectives

- Locate the lesion within the joint, tendon sheath, or bursa
- Explain how a CSF1 alteration produces a macrophage-rich tumor
- Distinguish localized from diffuse growth patterns
- Correlate morphology with clinical behavior and treatment limits

Joint tumors: The diagnostic setting

- Joint- and tendon-sheath lesions are often reactive rather than neoplastic
- Ganglion and synovial cysts are common mimics in this compartment
- True primary joint neoplasms are uncommon and frequently benign

Initial question

Is the lesion reactive or neoplastic — and where does it arise?

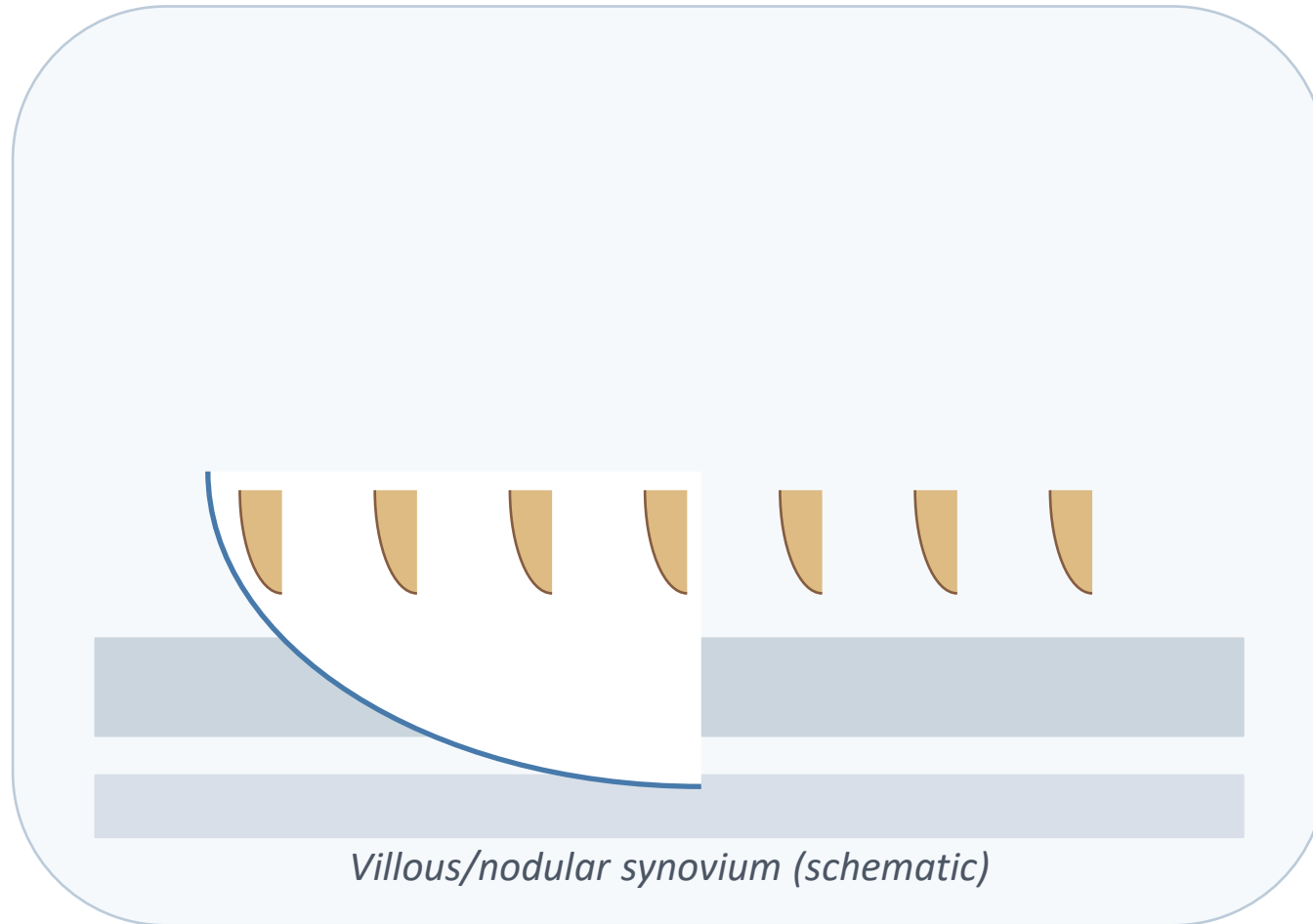
The central definition

Tenosynovial giant cell tumor is a benign synovium-associated neoplasm.

- Origin: Synovial lining of joints, tendon sheaths, or bursae
- Two biologically linked patterns: Localized and diffuse
- Benign designation does not exclude locally damaging growth

Three potential sites of origin

- Joint synovium
- Tendon sheath
- Bursal synovial lining



Two types of tenosynovial giant cell tumor

Feature	Localized	Diffuse
Typical form	Discrete nodule	Extensive synovial proliferation
Common setting	Hand tendon sheath	Large joint
Clinical theme	Painless, slow growth	Mechanical joint symptoms
Course	Less recurrence	Recurrence common

Age distribution

- Both localized and diffuse types are most often diagnosed in the second through fourth decades
- Age is a contextual clinical clue—not sufficient by itself for diagnosis
- Anatomic location and growth pattern remain more discriminating features

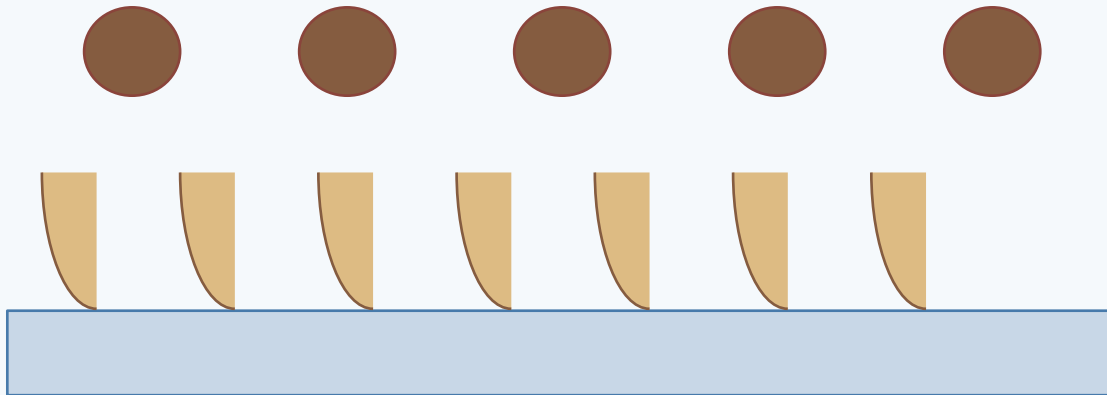
Historical terminology

“Pigmented villonodular synovitis” is the former name for diffuse TGCT.

- “Pigmented”: Prominent hemosiderin-containing cells
- “Villous/nodular”: Folded and nodular synovium
- Modern terminology emphasizes a neoplasm rather than merely synovitis

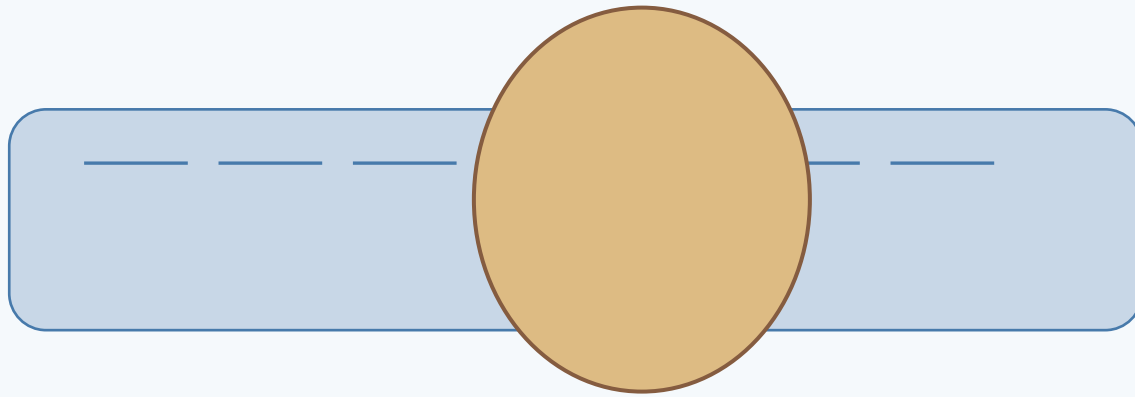
Diffuse type: The joint-centered pattern

- Expansive synovial involvement
- Tendency to involve larger joints
- Potential invasion of subsynovial tissue



Surface expansion with subsynovial spread (schematic)

Localized type: A tendon-sheath nodule



Nodule adjoining tendon sheath (schematic)

- Discrete nodular mass
- Usually attached to tendon sheath
- Hand is a characteristic location

Why anatomical context matters

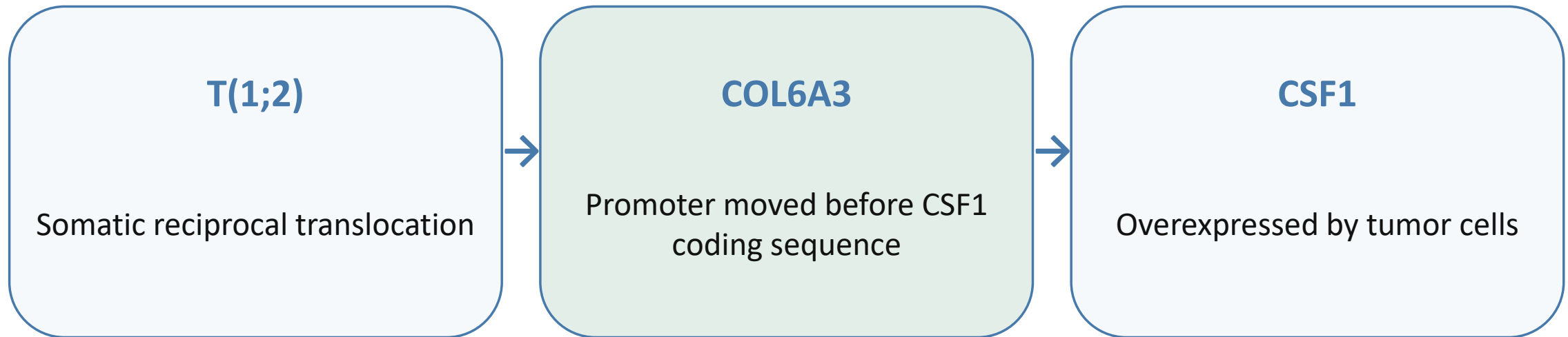
Question	Localized presentation	Diffuse presentation
What is found?	A single nodule	Synovial folds and nodules
Where?	Wrist and finger sheaths	Often knee
Clinical clue	Slow painless enlargement	Pain, locking, recurrent swelling

CSF1 biology is the pathogenetic core

The tumor recruits many macrophages; The neoplastic cells need not be numerically dominant.

- Genomic rearrangement alters CSF1 expression
- Neoplastic cells secrete excess M-CSF
- Macrophages expand in response to this signal

A genetic event initiates the process



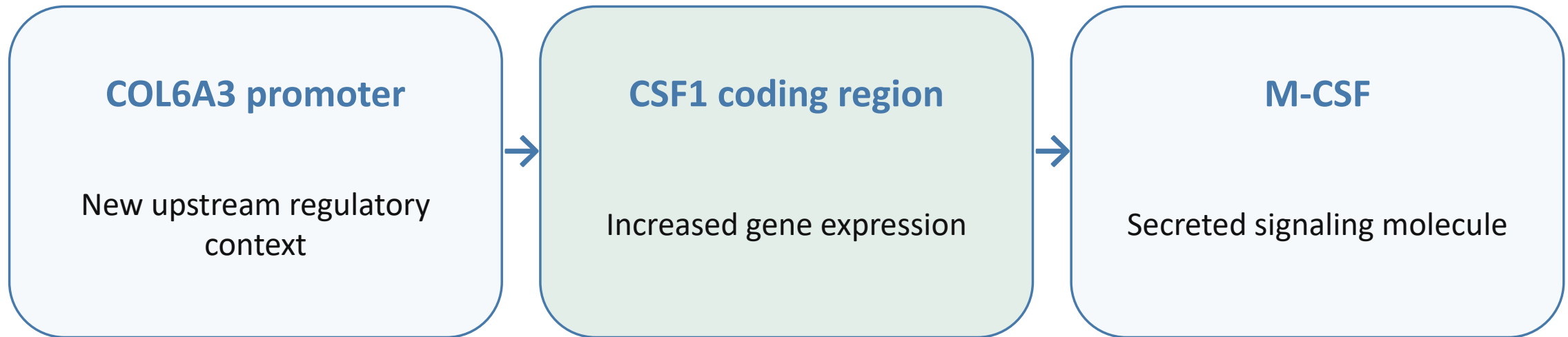
Schematic of promoter rearrangement; Not a depiction of chromosome band anatomy.

What the translocation specifies

T(1;2)(p13;q37) juxtaposes the COL6A3 promoter and CSF1 coding region.

- Somatic: Acquired in the tumor rather than inherited by definition
- Involves chromosome 1 and chromosome 2
- Occurs in the pathogenesis described for both morphologic types

Promoter-to-effector relationship

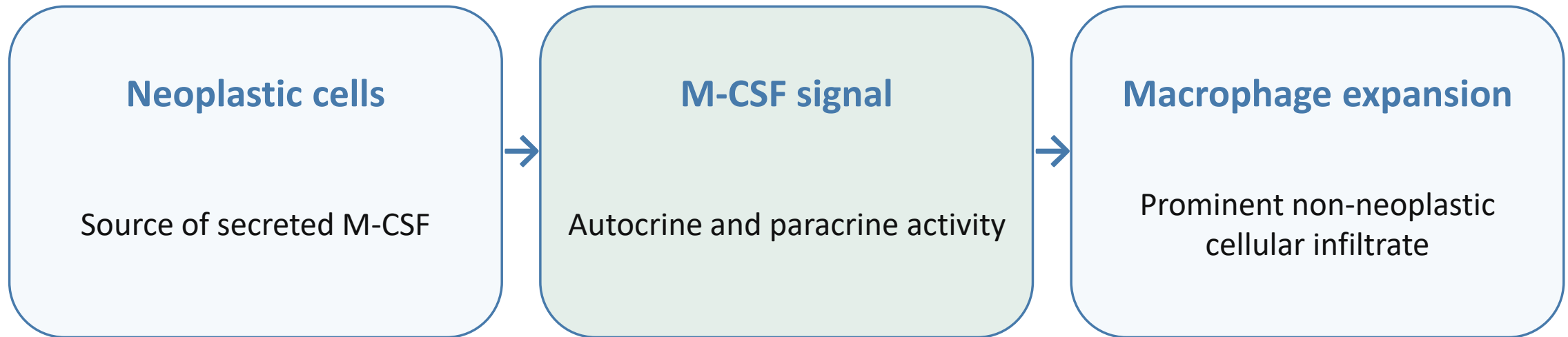


The Robbins account describes increased expression, not a new chimeric CSF1 protein.

CSF1 and M-CSF: One molecular axis

- CSF1 is the gene encoding macrophage colony-stimulating factor (M-CSF)
- In the rearranged tumor cells, M-CSF is overexpressed and secreted
- Its biological effects include stimulation of macrophage proliferation

How a minority builds a large lesion

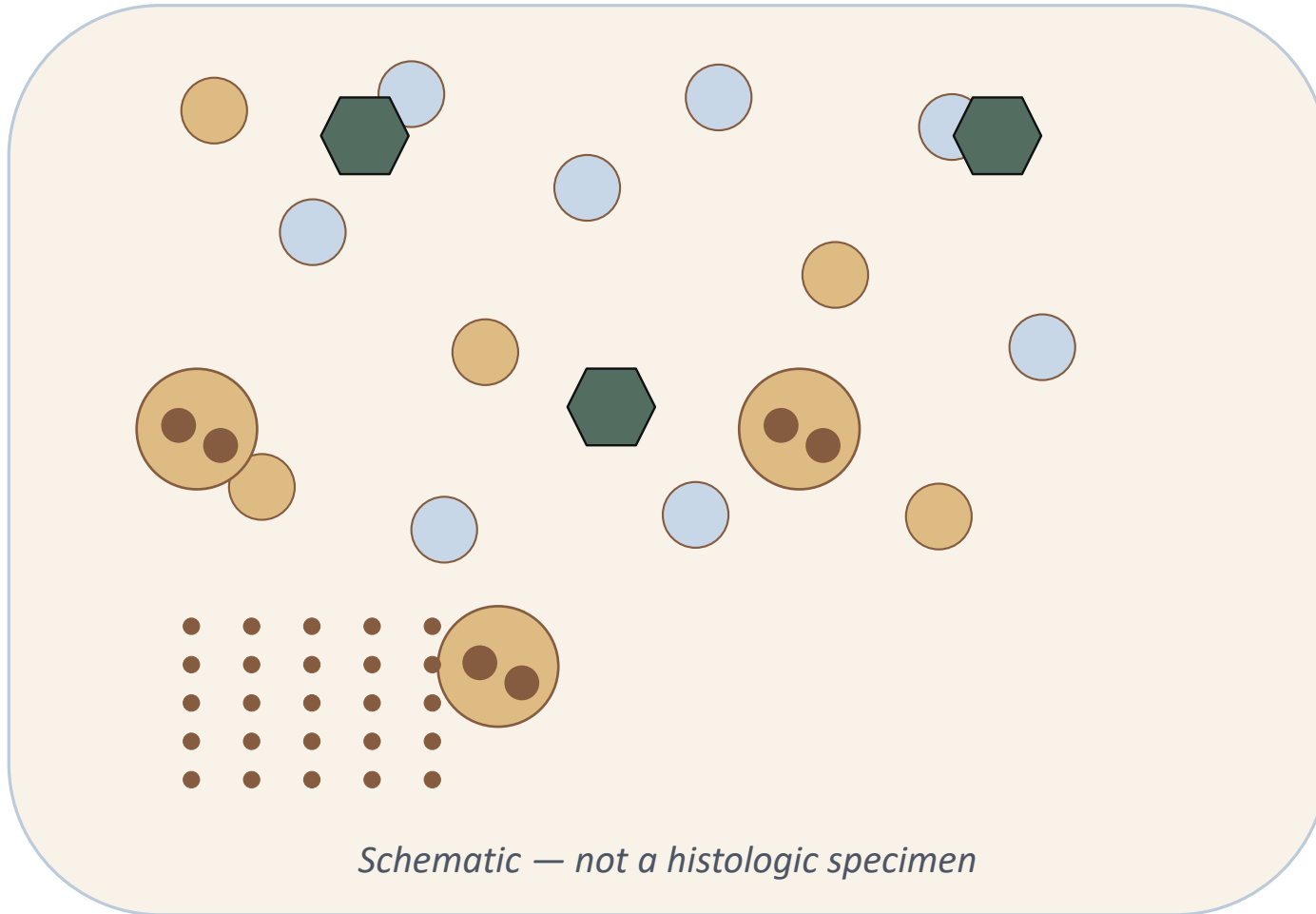


A macrophage-rich mass can be driven by a comparatively small altered cell population.

Autocrine and paracrine signaling

Mode	Direct target	Meaning in the tumor
Autocrine	Source cell itself	M-CSF acts on secreting neoplastic cells
Paracrine	Nearby cells	M-CSF acts on recruited macrophages

Tumor composition: Neoplastic minority



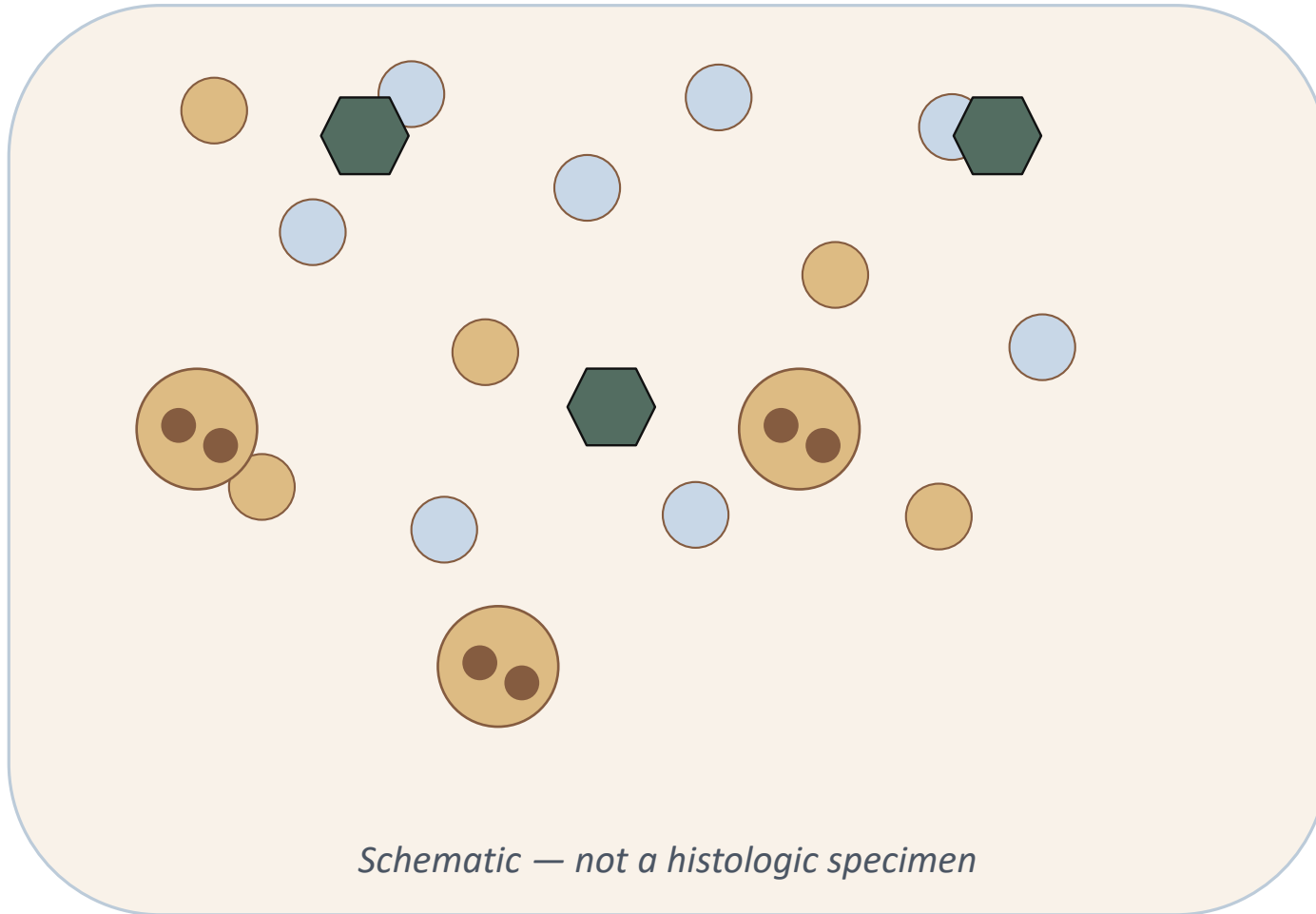
- Polygonal neoplastic cells are relatively few
- Numerous macrophages surround them
- Cellularity alone cannot identify the clone

Neoplastic

Macrophage

Giant cell

A macrophage-rich microenvironment



- M-CSF stimulates macrophage proliferation
- Macrophage accumulation dominates the tissue response
- Macrophages may occur in multinucleated forms

◆ Neoplastic

● Macrophage

● Giant cell

Morphology follows the signaling biology

Abundant macrophages are a biological consequence of CSF1 pathway activity.

- The molecular driver resides in neoplastic tumor cells
- The microscopic field includes many secondary participants
- This resolves the apparent mismatch between clone size and mass size

Neoplastic and recruited components

Property	Neoplastic tumor cells	Recruited macrophages
Relative abundance	Minority	Densely infiltrating population
Appearance	Polygonal; Synoviocyte-like	Hemosiderin-rich or foamy; Can be giant
Role	Overexpress M-CSF	Respond to CSF1 pathway signal

Both variants share the molecular mechanism

- The same CSF1-associated rearrangement in localized and diffuse forms
- This is consistent with their common microscopic cellular components
- The major distinction is growth distribution and clinical course

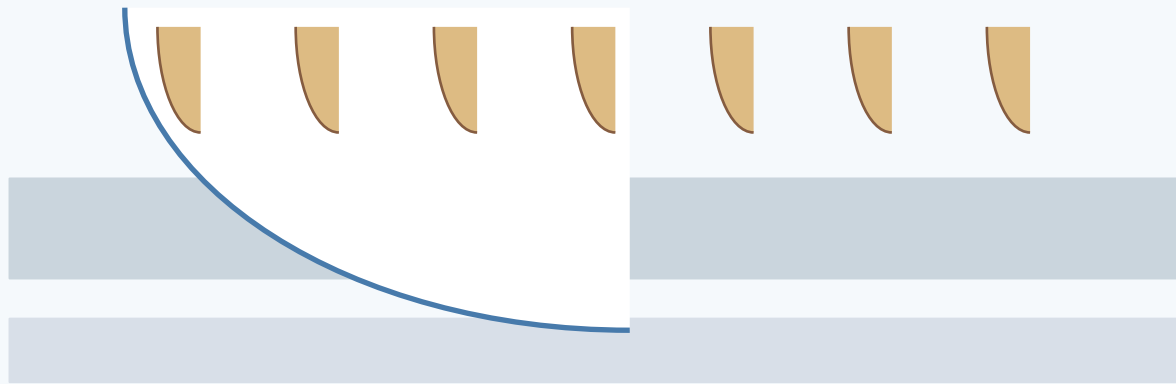
The gross specimen: Color as a clue

TGCT is described grossly as red-brown to orange-yellow.

- Pigment-laden macrophages contribute to the characteristic appearance
- Diffuse disease produces a folded or nodular synovial surface
- Color is helpful but not a stand-alone diagnostic criterion

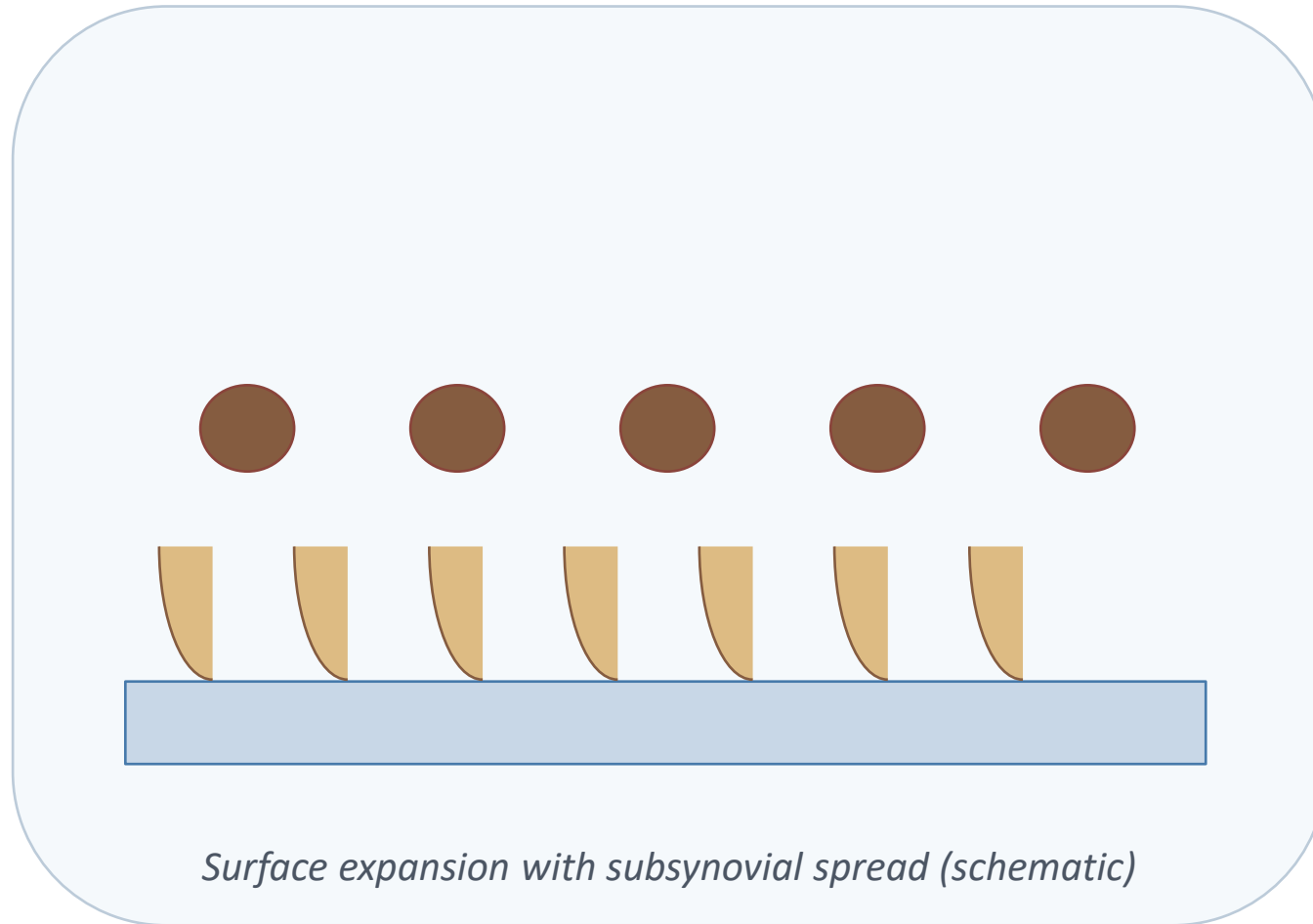
Diffuse gross morphology: Villous synovium

- Smooth synovium becomes a tangled mat
- Red-brown folds and finger-like projections
- Multiple nodules can coexist



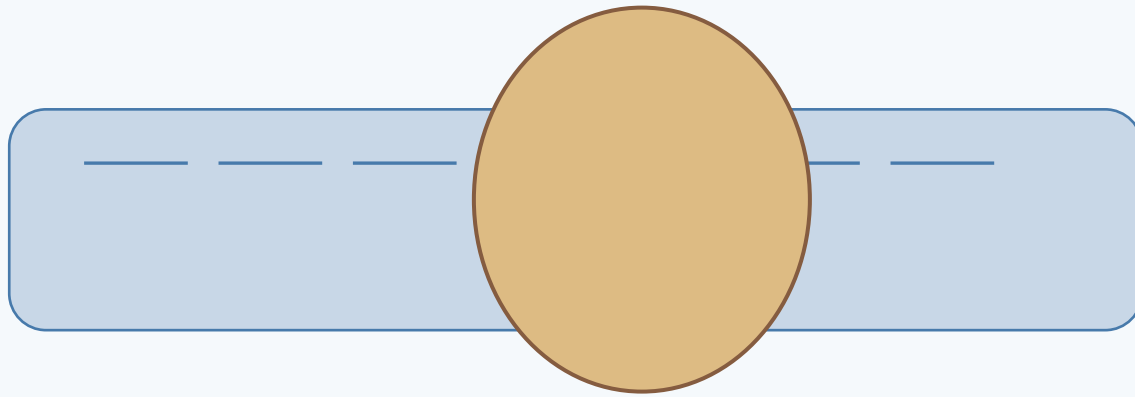
Villous/nodular synovium (schematic)

Diffuse involvement is architectural



- Surface proliferation extends along synovium
- Subsynovial infiltration is described
- Distribution contributes to local complexity

Localized gross morphology: Circumscribed



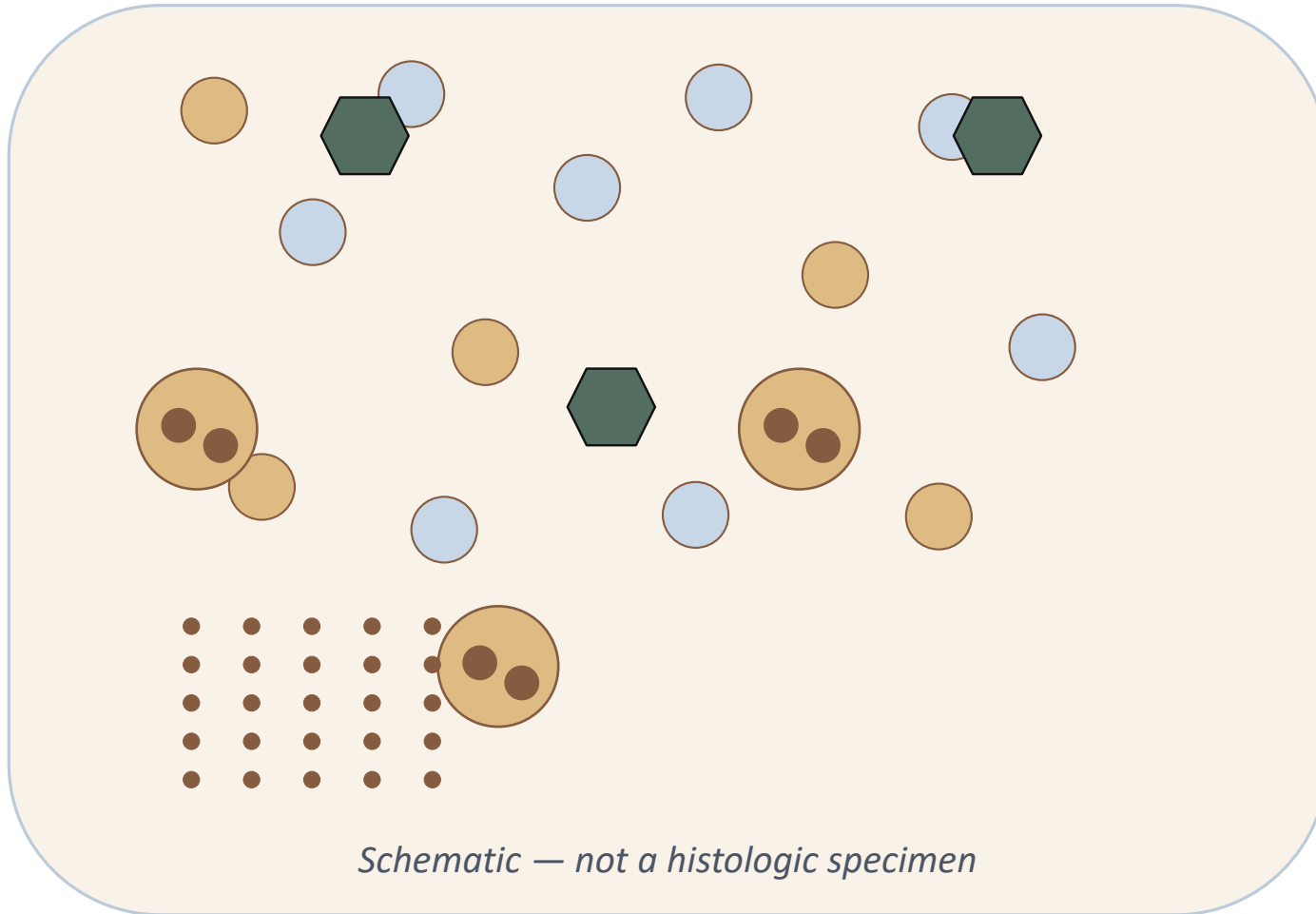
Nodule adjoining tendon sheath (schematic)

- Well-defined localized nodule
- Often arises adjacent to a tendon sheath
- Distinct from widespread joint-surface replacement

A pedicle can connect the mass to synovium

- A solid aggregate may remain attached to synovium by a pedicle
- Pedunculation is an architectural finding, not proof of benignity alone
- Interpret attachment together with the cell population

Recognizing synoviocyte-like cells



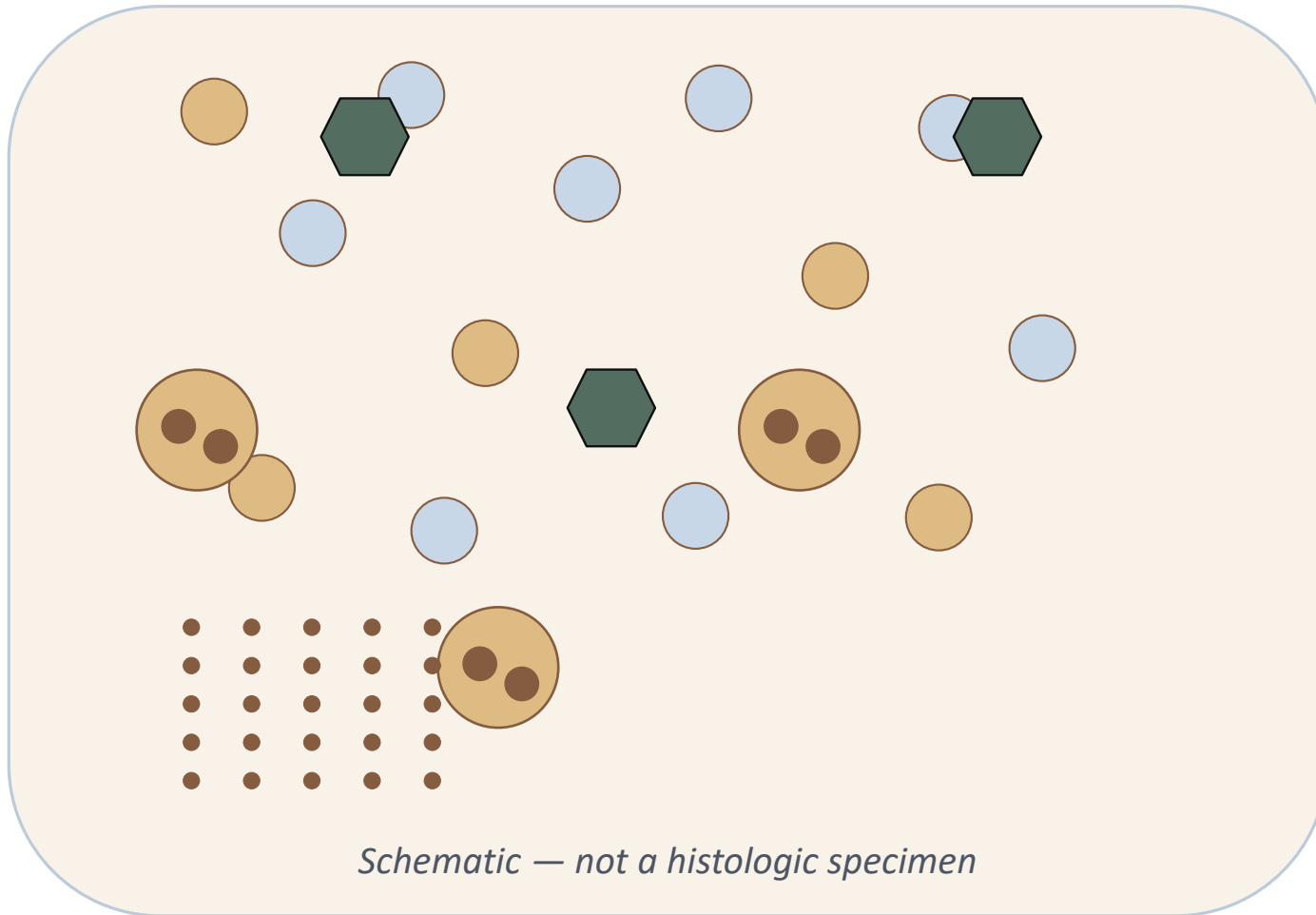
- Moderately sized polygonal neoplastic cells
- Appearance resembles synoviocytes
- These cells form a minority of the lesion

● Neoplastic

● Macrophage

● Giant cell

Macrophages with hemosiderin



- Hemosiderin may accumulate within macrophages
- Pigmented cells help explain red-brown appearance
- Not every pigmented cell is a neoplastic cell

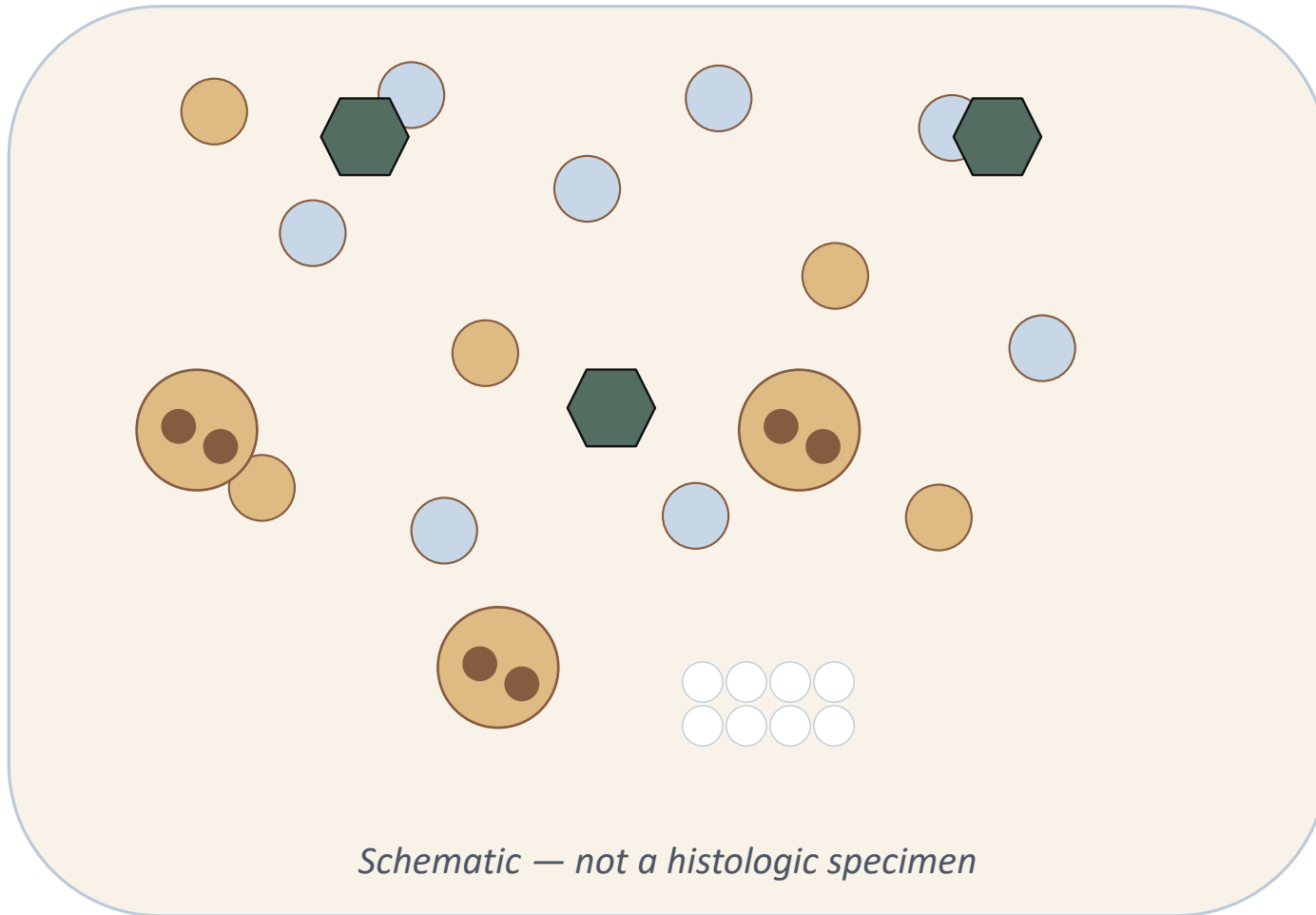
● Neoplastic

● Macrophage

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Foamy macrophages

- Macrophages can contain foamy lipids
- Foamy histiocytes occur alongside other cell types
- Mixture is expected in both variants

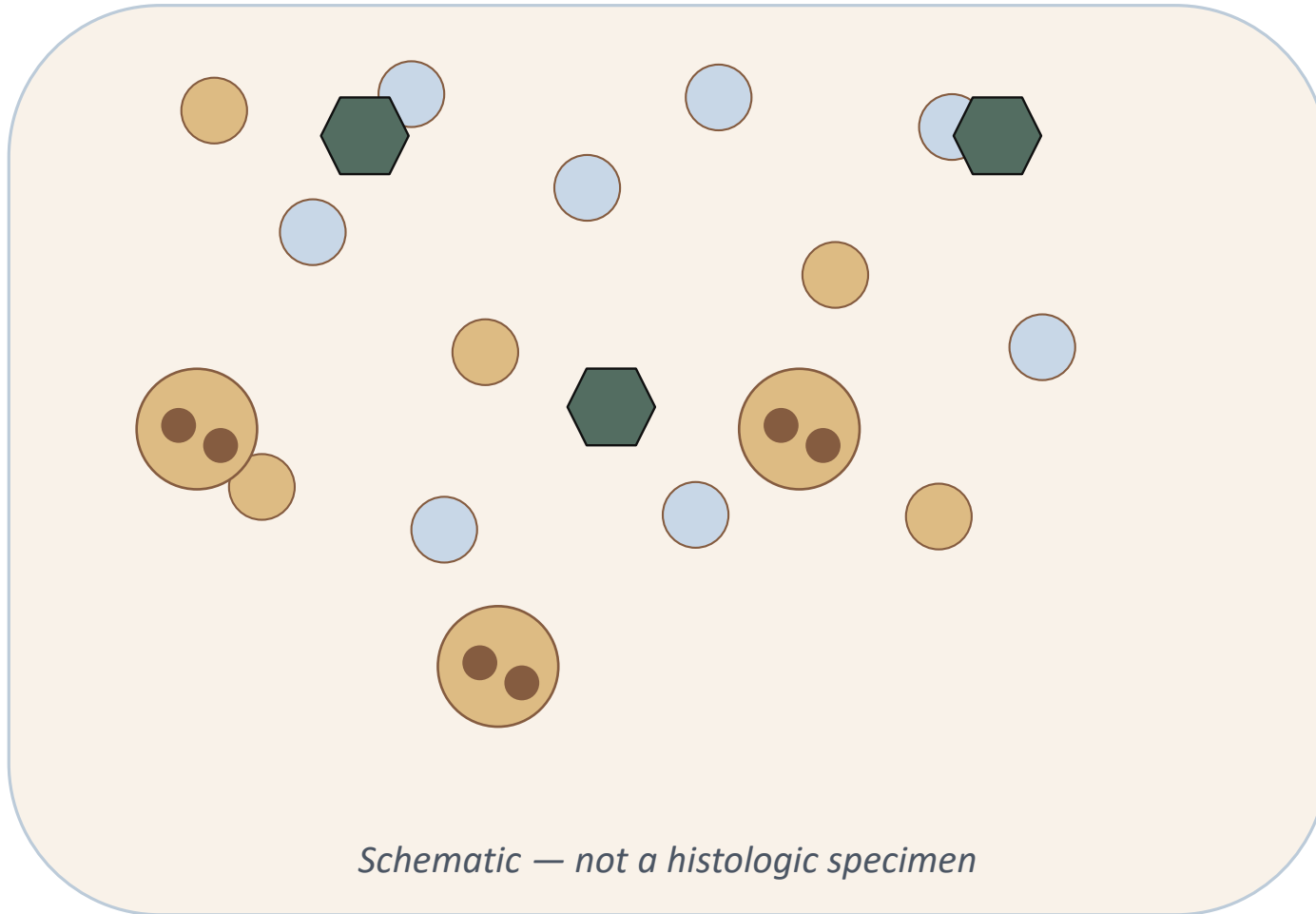


Neoplastic

Macrophage

Giant cell

Multinucleated giant cells



- Macrophages may become multinucleated
- Giant cells are a conspicuous component
- Presence alone does not define the neoplastic clone

● Neoplastic

● Macrophage

● Giant cell

Older lesions may become fibrotic

Fibrosis is part of the described histologic evolution of TGCT.

- Longer-standing tumors need not show only a cellular architecture
- Fibrotic regions may coexist with macrophage-rich areas
- A limited field may underrepresent the whole lesion

Microscopic checklist

Component	Expected observation	Interpretive significance
Tumor population	Polygonal synoviocyte-like cells	Neoplastic minority
Histiocytes	Hemosiderin or foamy lipid	Macrophage recruitment
Giant cells	Multinucleated forms	Macrophage-lineage component
Stroma	Possible fibrosis	Older-lesion change

Histologic geography differs

Finding	Localized TGCT	Diffuse TGCT
Macrophage infiltrate	Present	Present
Giant cells	Can be present	Can be present
Overall growth	Discrete / circumscribed	Synovial spread and subsynovial invasion

Pathologic interpretation requires distribution

The same basic cell mixture can occur in two different architectural patterns.

- Do not classify type using macrophages or giant cells alone
- Examine whether growth is discrete or diffusely synovial
- Integrate specimen anatomy with the clinical presentation

Gross–microscopic correlation

Gross appearance	Tissue correlate
Red-brown tissue	Hemosiderin-containing macrophages
Villous/nodular synovium	Broad surface proliferation
Circumscribed mass	Localized nodular architecture
Fibrotic older lesion	Stromal fibrosis

Diffuse TGCT: Knee predominance

That 80% of diffuse presentations occur in the knee.

- The knee is therefore a high-yield site in clinical vignettes
- Other large joints can still be involved
- Site is a probability clue—not a diagnostic criterion

Diffuse clinical presentation

- Pain is a common presenting symptom
- Locking is described, consistent with intra-articular mechanical disturbance
- Recurrent swelling may dominate the clinical history
- Some patients also have a palpable mass

Why diffuse TGCT mimics monoarthritis

Clinical feature	Potential interpretation
Recurrent single-joint swelling	May be mistaken for monoarticular arthritis
Pain with episodic locking	Suggests an intra-articular process
Mass or erosive extension	May suggest another neoplasm

Atypical but important: Extension and erosion

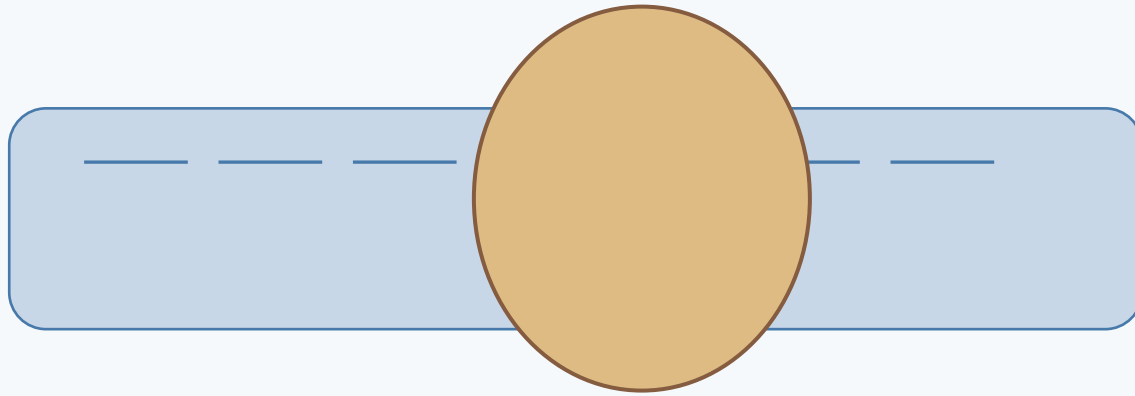
- Some diffuse lesions erode into adjacent bone
- Soft-tissue extension can also occur
- Locally destructive growth may resemble other neoplasms
- Benign classification must not be confused with harmless behavior

Diffuse lesions frequently recur

Recurrence is a prominent clinical problem for the diffuse form.

- Broad synovial distribution complicates disease extent
- A locally infiltrative pattern coexists with benign histologic designation
- Clinical surveillance is therefore a relevant management consideration

Localized disease: The wrist and fingers



Nodule adjoining tendon sheath (schematic)

- Solitary nodule
- Slow growing and usually painless
- Frequent in tendon sheaths of digits or wrist

Localized TGCT: Expected behavior

- Most often presents as a discrete, slow-growing painless mass
- Bone erosion is less common than in diffuse disease
- Recurrence is also less common than in diffuse disease

Comparison of expected clinical behavior

Feature	Localized	Diffuse
Mass pattern	Solitary nodular mass	Broad synovial disease
Symptoms	Often painless	Pain, locking, swelling
Bone erosion	Less common	Can occur
Recurrence	Less common	Common

Benign does not imply biologically inert

TGCT illustrates why neoplasm grade and local impact are separate questions.

- The tumor is classified as benign
- Diffuse lesions may erode bone and infiltrate soft tissues
- Treatment decisions therefore consider function and morbidity

Ganglion cyst versus TGCT

Aspect	Ganglion cyst	Tenosynovial giant cell tumor
Category	Degenerative cystic lesion	Benign neoplasm
Tissue content	Synovial-like fluid	Cellular mass
Wall / cells	No true cell lining	Neoplastic cells + macrophages
Common site	Near wrist joint or sheath	Hand sheath in localized TGCT

Synovial cyst versus TGCT

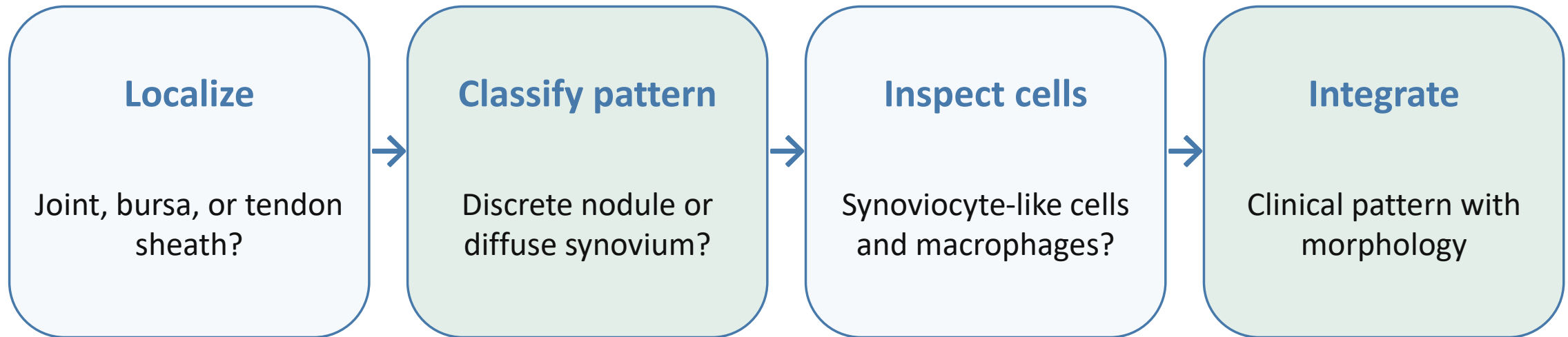
Aspect	Synovial cyst	Tenosynovial giant cell tumor
Origin	Synovial herniation / enlarged bursa	Synovium-associated neoplasm
Structure	Synovium-like lining, fluid	Tumor-cell and macrophage mixture
Context	Can occur with RA or OA	Neoplastic CSF1 signaling described

Compartment-based differential reasoning

The location of a nodule is a starting point, not the diagnosis.

- A wrist mass can be a ganglion or localized TGCT
- Fluid-filled lined/unlined cysts differ from a cellular neoplasm
- Specimen architecture and cellular composition resolve the distinction

A practical tissue-identification sequence

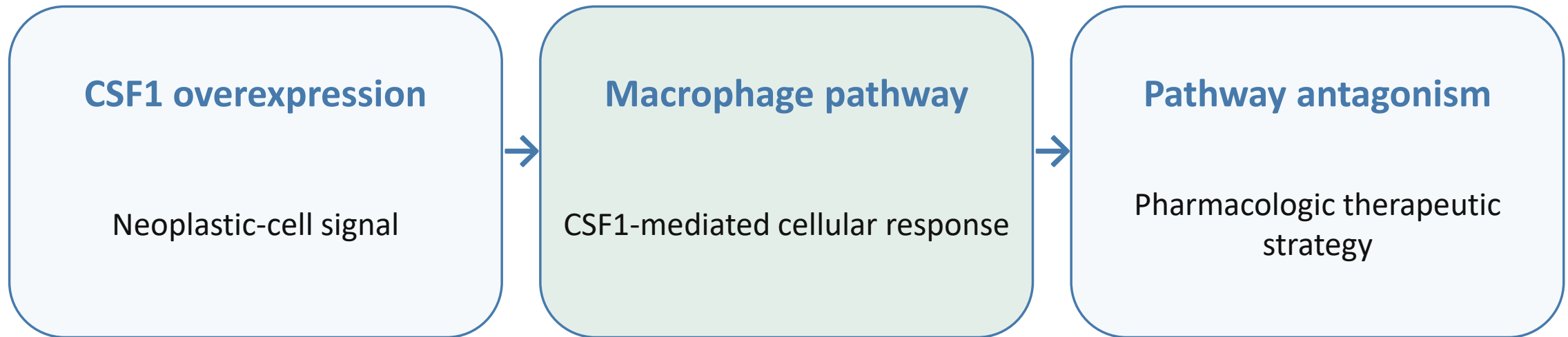


This is an educational interpretation pathway; No diagnostic test-performance claims are implied.

Excision remains the central treatment

- Surgical excision is described as the mainstay of treatment
- The extent and distribution of disease matter for treatment impact
- A localized nodule and widespread synovial disease pose different practical challenges

Why CSF1-directed therapy is plausible



Mechanism-to-therapy rationale; Not a drug-specific efficacy or dosing claim.

A major therapeutic constraint: Liver toxicity

Antagonists of M-CSF signaling can cause severe hepatotoxicity.

- Them as effective, but not routine therapy for every patient
- Risk–benefit assessment is essential
- Use is restricted to cases in which surgery risks substantial morbidity or functional impairment

Treatment principles by disease context

Clinical situation	Management implication
Resectable tumor	Surgical excision is the mainstay
Surgery may cause major functional loss	CSF1-pathway antagonism may be considered
Considering systemic antagonism	Severe hepatotoxicity risk must be weighed

Case 1: Recurrent knee symptoms

Illustrative case

An adult has recurrent knee swelling, pain, and locking. A synovium-based nodular proliferation is identified.

Question: Which TGCT growth pattern is most consistent with the presentation?

Case 1: Interpretation

Illustrative case

A joint-wide, folded synovium with macrophage-rich tumor is encountered.

Diffuse TGCT is favored: Large-joint pattern, synovial spread, and characteristic symptoms.

Case 2: Slow-growing finger mass

Illustrative case

An adult has a solitary, painless, slowly enlarging nodule closely associated with a finger tendon sheath.

Question: What morphology and clinical behavior are most expected?

Case 2: Interpretation

Illustrative case

The excised lesion is well circumscribed and contains synoviocyte-like cells with macrophages and giant cells.

Localized TGCT fits; Bone erosion and recurrence are less common than in diffuse disease.

Case 3: A pigmented, cell-rich mass

Illustrative case

A microscopic sample contains many hemosiderin-laden macrophages and multinucleated giant cells. Only scattered polygonal synoviocyte-like cells are present.

Question: Which population is expected to carry the neoplastic CSF1 alteration?

Case 3: Interpretation

Illustrative case

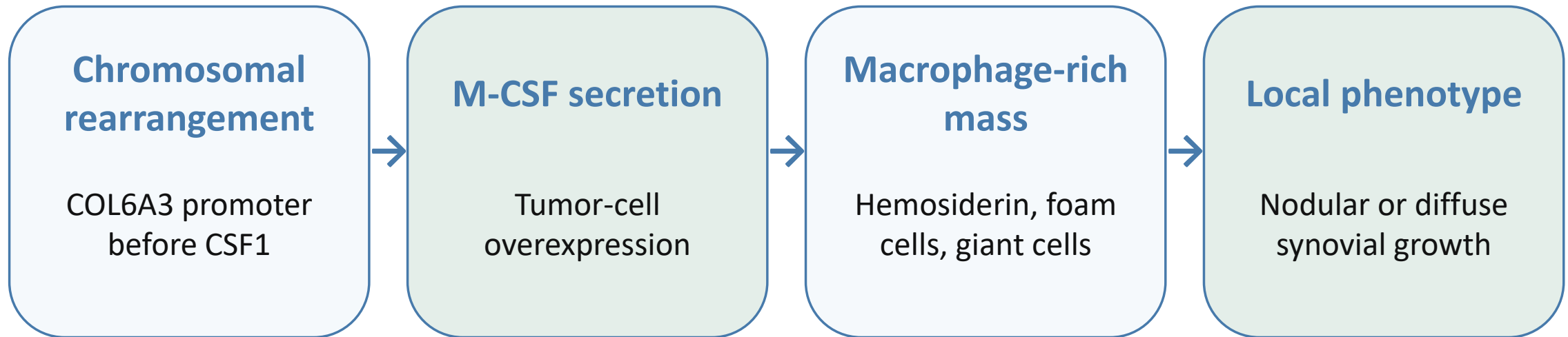
The abundant macrophages are the most obvious cells under the microscope.

The relatively rare neoplastic cells drive M-CSF expression and macrophage recruitment.

High-yield consolidation: The two types

Dimension	Localized TGCT	Diffuse TGCT
Gross	Well-circumscribed nodule	Villous / nodular synovium
Preferred compartment	Tendon sheath of hand	Large joint; Often knee
Microscopy	Tumor cells + macrophages	Shared mixture; Infiltrative extent
Clinical course	Less erosion / recurrence	Pain, swelling, locking; Recurrence

The complete pathogenetic model



Interpretation links directly to the morphologic and clinical descriptions.

Five defensible conclusions

- TGCT is a benign tumor of synovium-related structures
- Localized and diffuse types share a CSF1-based mechanism
- The true neoplastic population can be a minority of the mass
- Diffuse disease is synovial, locally damaging, and prone to recurrence
- Surgery is central; CSF1 antagonism is limited by toxicity

Primary reference

Robbins, Cotran & Kumar

Pathologic Basis of Disease · 11th edition

“Tenosynovial Giant Cell Tumor”

Gross and microscopic sketches in this lecture are original editable schematics, not actual pathology specimens.