

Laboratory testing of monoclonal gammopathy

What tests to order and how to interpret them

Presenter Disclosure

- **Faculty / Speaker's name: Arvand Barghi**
- **Relationships with commercial interests:**
 - **None**

Mitigating Potential Bias

- Not applicable

Learning Objectives

1. Review the structure and function of immunoglobulins and the patterns of polyclonal and monoclonal gammopathies
2. Discuss the laboratory tests pertaining to immunoglobulin investigation
3. Review the appropriate laboratory tests to order in the setting of screening for suspected plasma cell dyscrasia

Review of lab tests
pertaining to
immunoglobulin
status

Serum protein electrophoresis

Serum free light chains

Urine protein electrophoresis

Quantitative immunoglobulins

RESULTS

REF

SERUM MONOCLONAL PROTEIN INVESTIGATION

Serum Total Protein	78
Serum Albumin	37
IgG	16.40*
IgA	0.36*
IgM	0.22*

Monoclonal Immunoglobulin PRESENT

Class/type: Previous IgG / Kappa

Monoclonal Ig concentration: 14

NOTE: IgG, IgA and IgM results include normal and concentration when present.

Serum Electrophoresis

Immunology

Test	Result	Range
Immunoglobulin Light Chains Kappa Free	84.44 mg/L	3.30-19.40
Immunoglobulin Light Chains Lambda Free	52.60 mg/L	5.71-26.30
Immunoglobulin Light Chains Kappa Free/Immunoglobulin Light Chains Lambda Free	1.61 Ratio	0.26-1.65

Urine protein electrophoresis

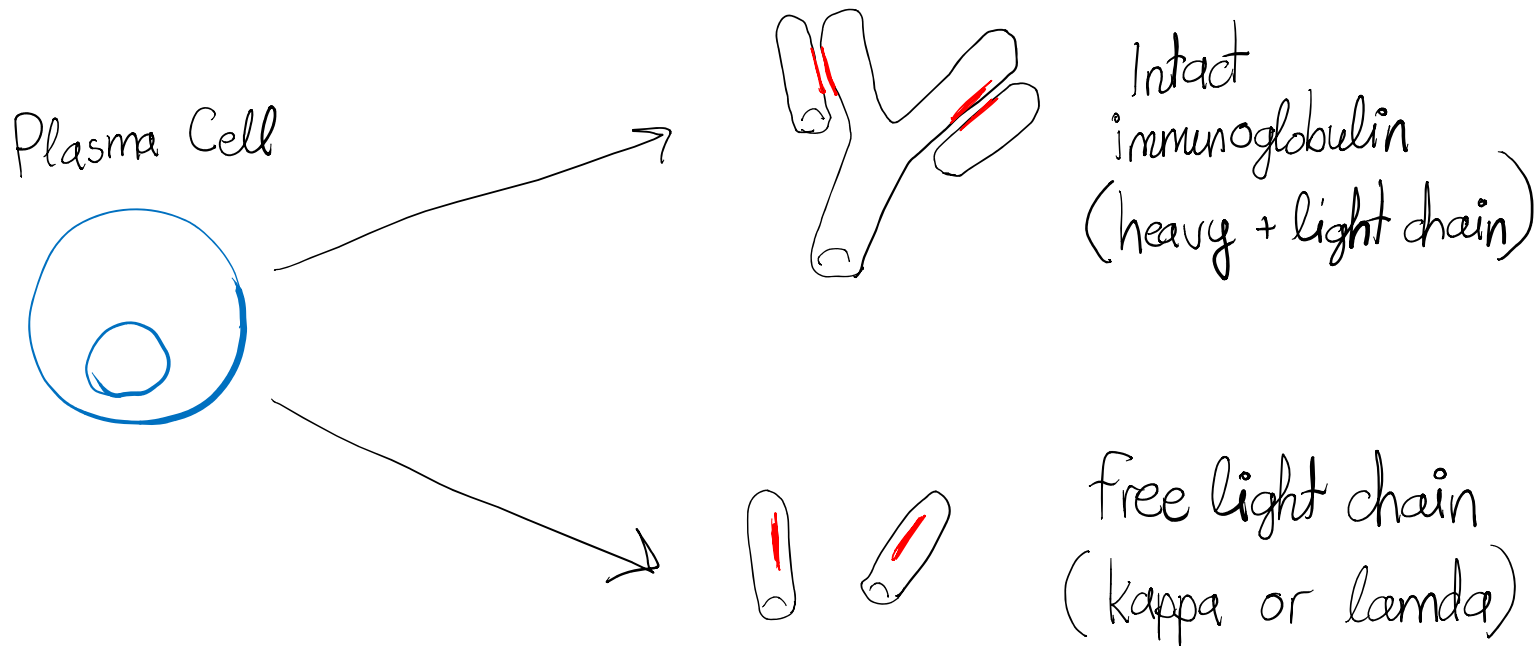
- Does not improve sensitivity of multiple myeloma screening over SPEP + SFLC¹
- Only valid if ordered on a 24 hour urine collection
 - Low adherence rates, less convenient

McTaggart MP, Lindsay J, Kearney EM. Replacing urine protein electrophoresis with serum free light chain analysis as a first-line test for detecting plasma cell disorders offers increased diagnostic accuracy and potential health benefit to patients. *Am J Clin Pathol*. 2013;140(6):890-897. doi:10.1309/AJCP25IHYLEWCAHJ

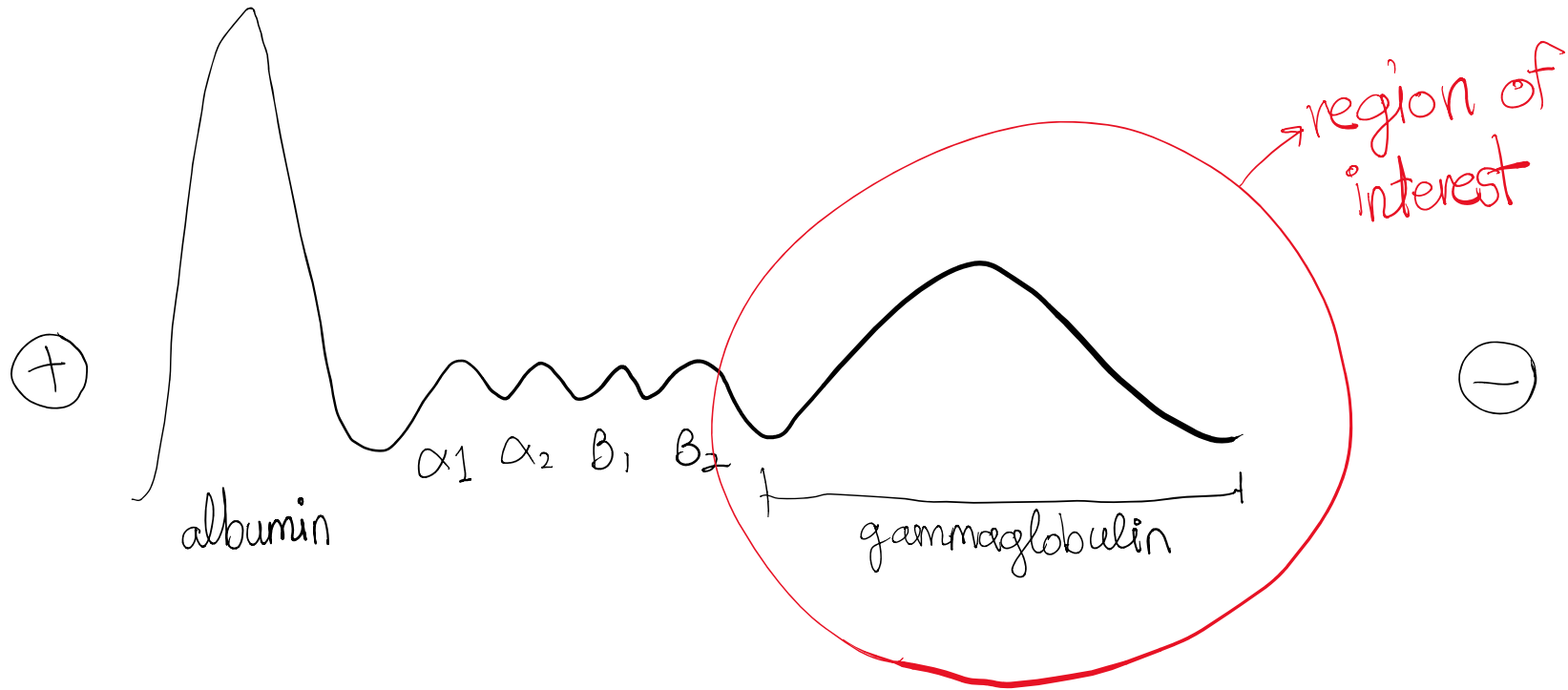
Quantitative immunoglobulins

- Reports quantitative amount of IgG, IgA, IgM
 - Elevated in inflammatory states
- Does not help to determine clonality
- Not required as part of the screening test for a patient suspected of multiple myeloma

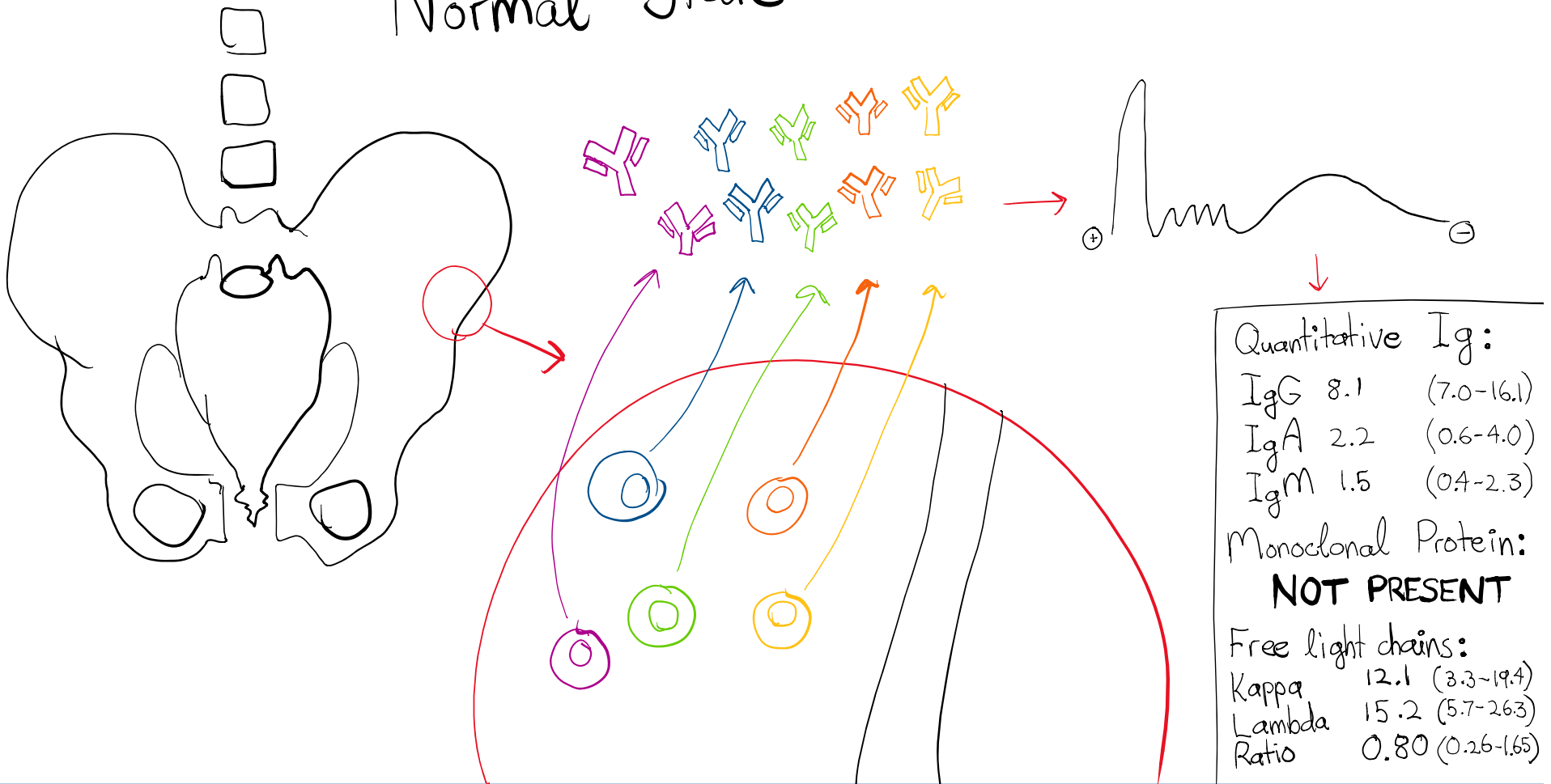
Plasma cell function



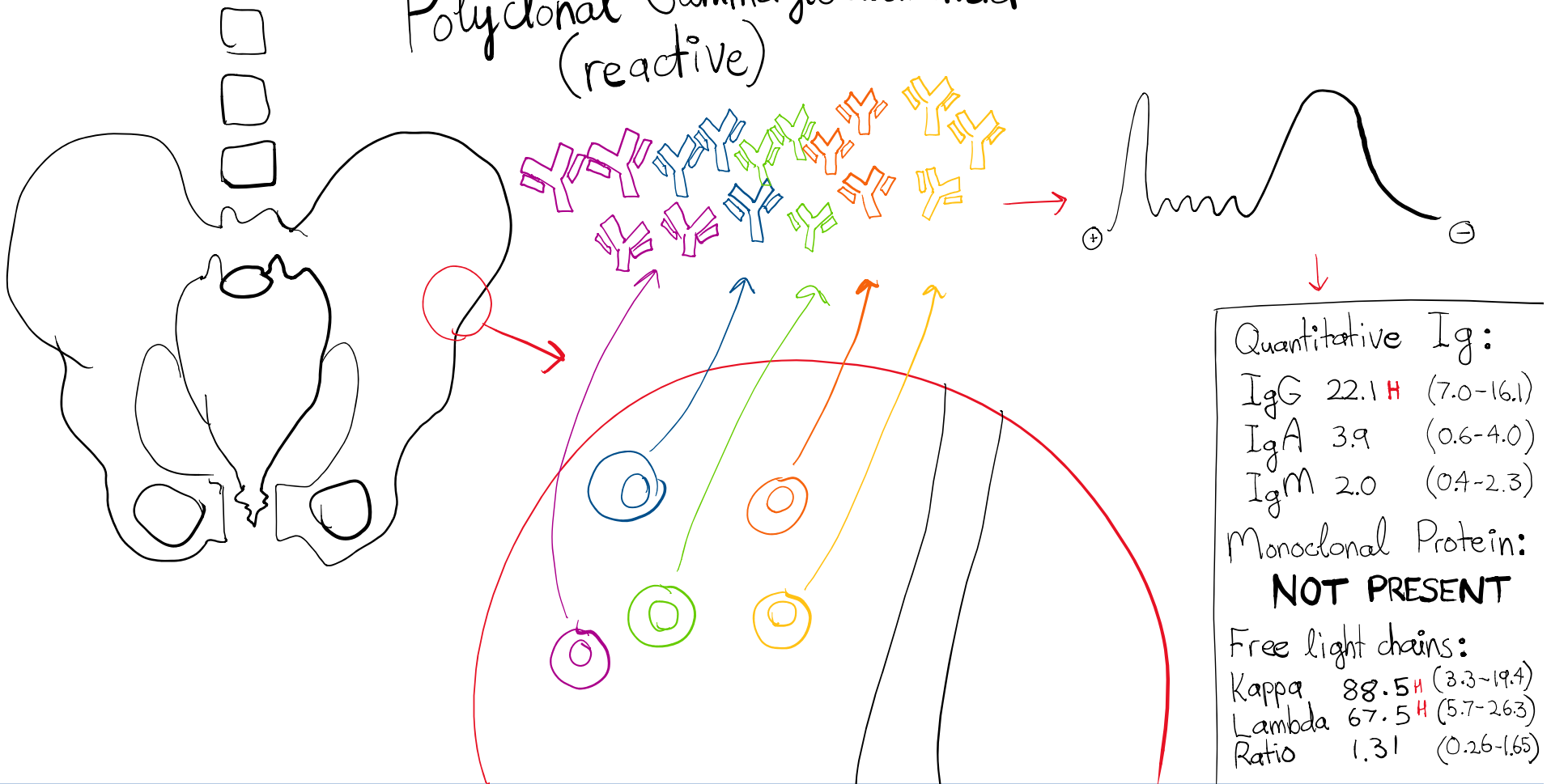
Serum protein electrophoresis (SPEP)



Normal State



Polyclonal Gammaglobulinemia (reactive)



Quantitative Ig:

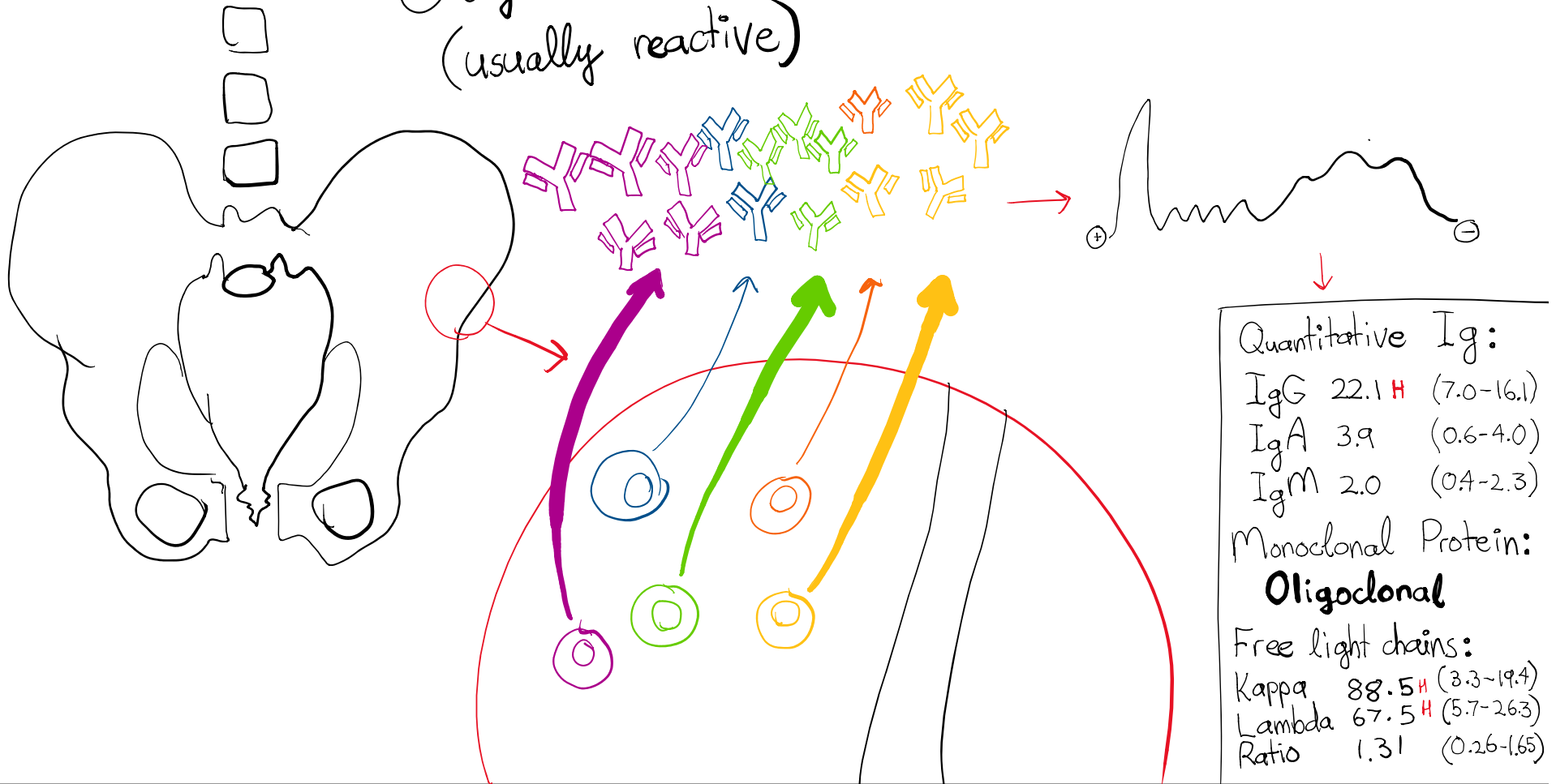
IgG	22.1 H	(7.0-16.1)
IgA	3.9	(0.6-4.0)
IgM	2.0	(0.4-2.3)

Monoclonal Protein:
NOT PRESENT

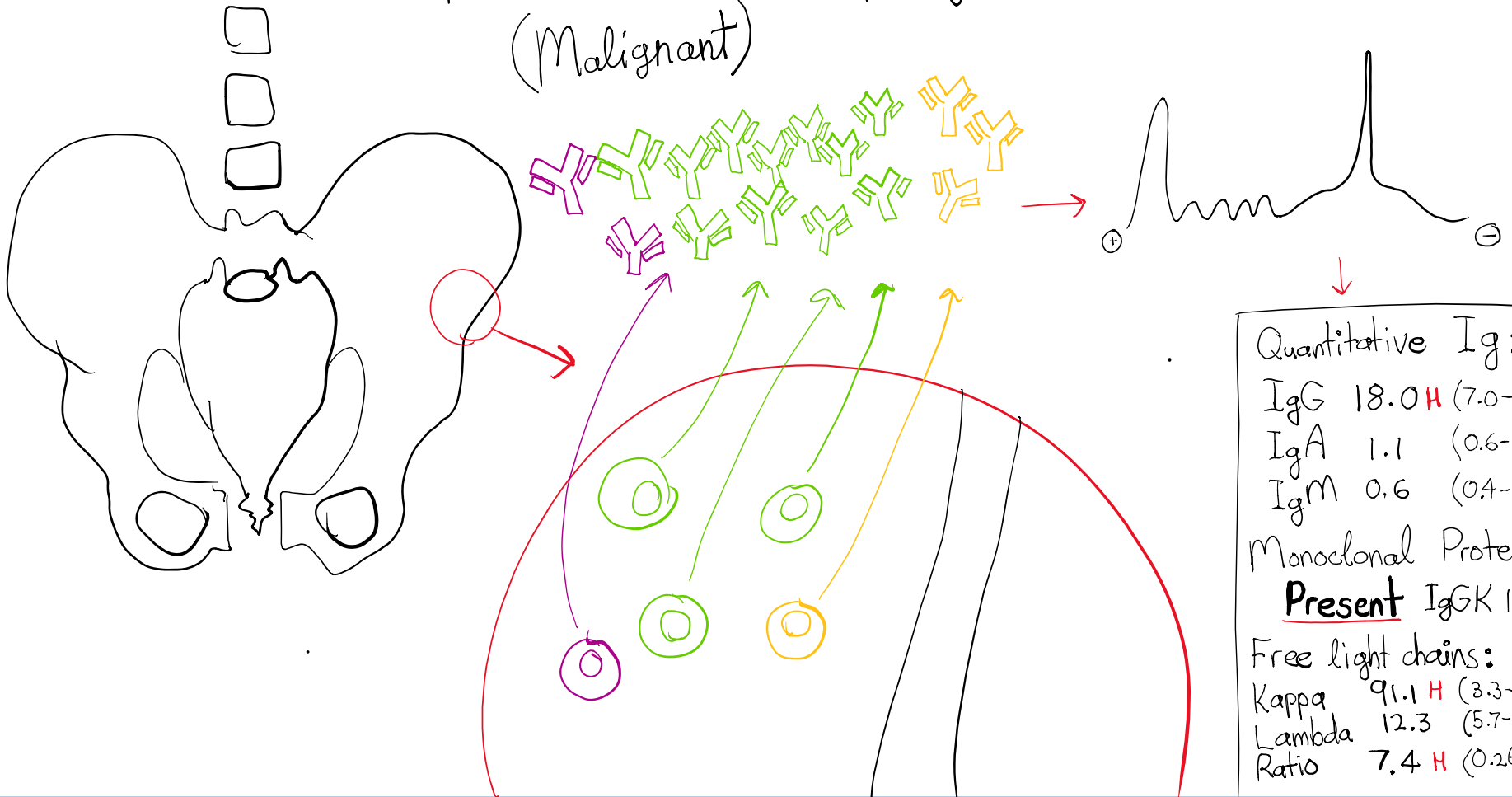
Free light chains:

Kappa	88.5 H	(3.3-19.4)
Lambda	67.5 H	(5.7-26.3)
Ratio	1.31	(0.26-1.65)

Oligoclonal Pattern (usually reactive)



Monoclonal Gammopathy (Malignant)



Quantitative Ig:

IgG	18.0 H	(7.0-16.1)
IgA	1.1	(0.6-4.0)
IgM	0.6	(0.4-2.3)

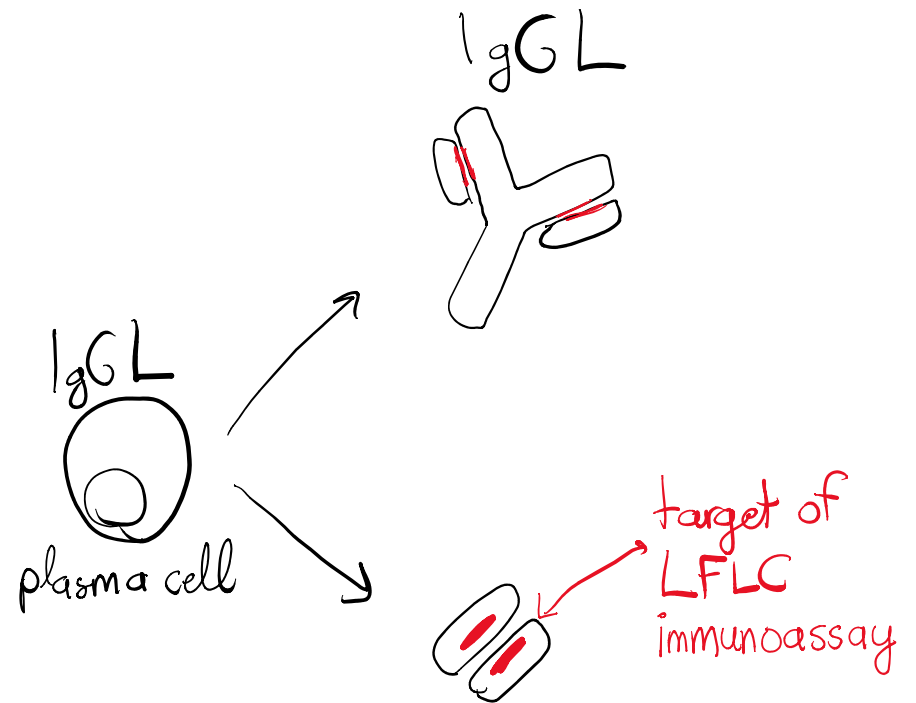
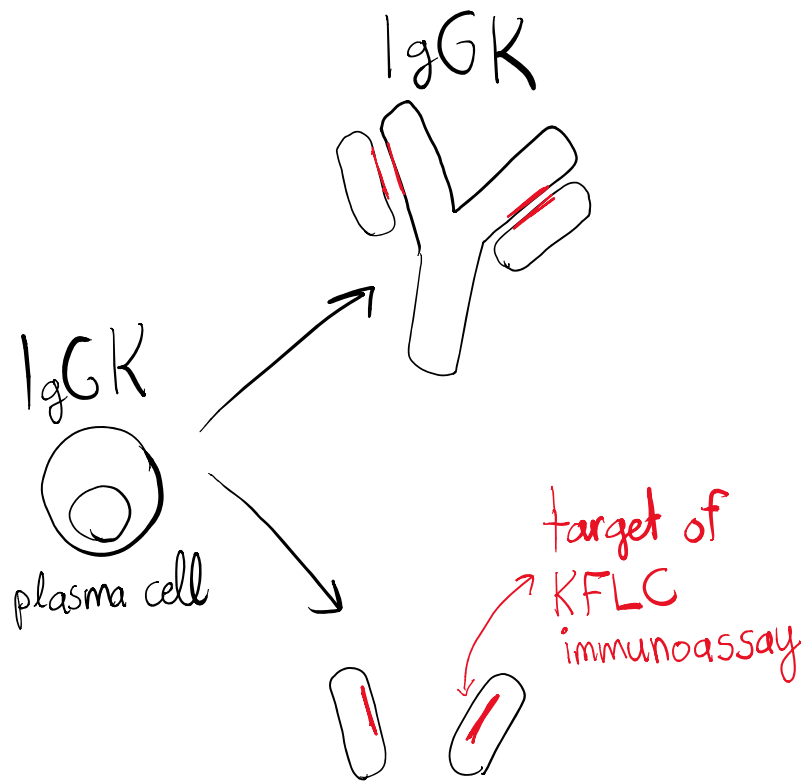
Monoclonal Protein:
Present IgGK 14g/L

Free light chains:

Kappa	91.1 H	(3.3-19.4)
Lambda	12.3	(5.7-26.3)
Ratio	7.4 H	(0.26-1.65)

Free light chain assay

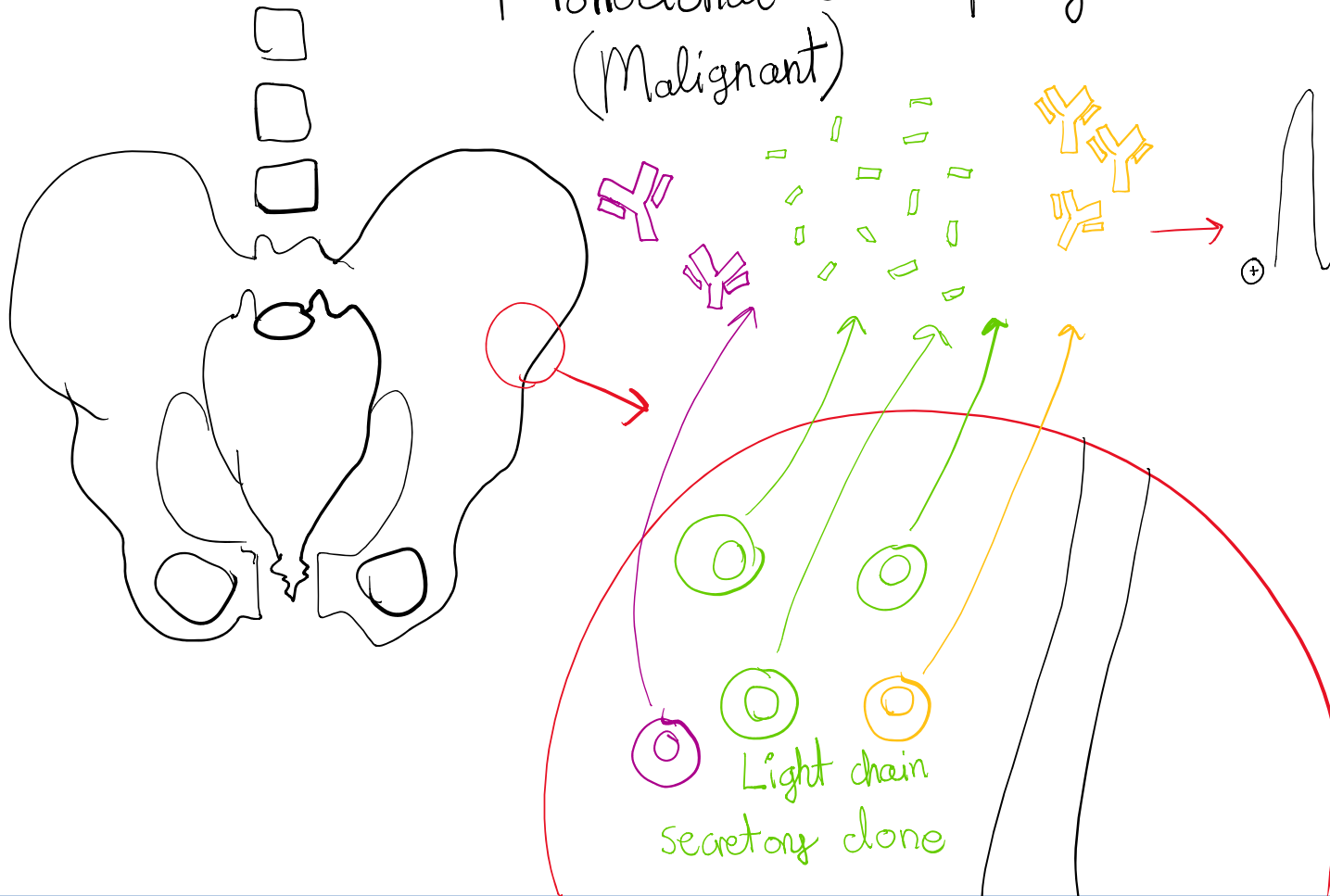
- Immuno-assay targeting the exposed epitope of circulating free light chains
- Free light chains are either kappa or lambda
- In reactive states (inflammation, infection), the free light chains will be elevated but the ratio should not be abnormal
- Normal ratio of kappa to lambda is 0.26-1.65
- In patients with chronic renal insufficiency $EGFR < 20$, the accepted normal range is 0.37-3.05
- Severely elevated free light chains in multiple myeloma lead to cast nephropathy



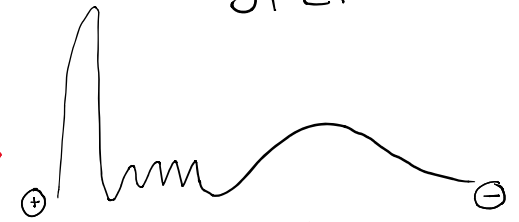
Light chain secretory multiple myeloma

- Malignant cell with deranged immune function
- Secretes free light chain (committed to either kappa or lambda) without secreting a viable heavy chain immunoglobulin into circulation
- Clonal proliferation of a light chain secretory clone will result in abnormality of the free light chain ratio, but with no detectable abnormality in the SPEP
- Light chain myeloma seen in 10-15% of cases

Monoclonal Gammopathy (Malignant)



Normal SPEP



↓

Quantitative Ig:		
IgG	8.1	(7.0-16.1)
IgA	2.2	(0.6-4.0)
IgM	1.5	(0.4-2.3)
Monoclonal Protein:		
NOT PRESENT		
Free light chains:		
Kappa	91.1 H	(3.3-19.4)
Lambda	12.3	(5.7-26.3)
Ratio	7.4 H	(0.26-1.65)

TESTS TO ORDER WHEN SUSPECTING MULTIPLE MYELOMA

SPEP + SFLC

Changes we have made

- SPEP and SFLC are now a paired test
- UPEP is now cancelled if ordered on a random specimen
- “Renal range” of SFLC ratio is reported as a comment
- 24 hour UPEP is restricted to workup of renal amyloidosis and clinical trials

Take home message(s)

- Order SPEP and SFLC for patients with suspected multiple myeloma
- Quantitative immunoglobulin assays do not infer clonality
- Abnormal ratios, not abnormal absolute values alone, suggest clonality on SFLC assay
- Don't order UPEP for suspected multiple myeloma
 - it will get cancelled in Manitoba

Thank you

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