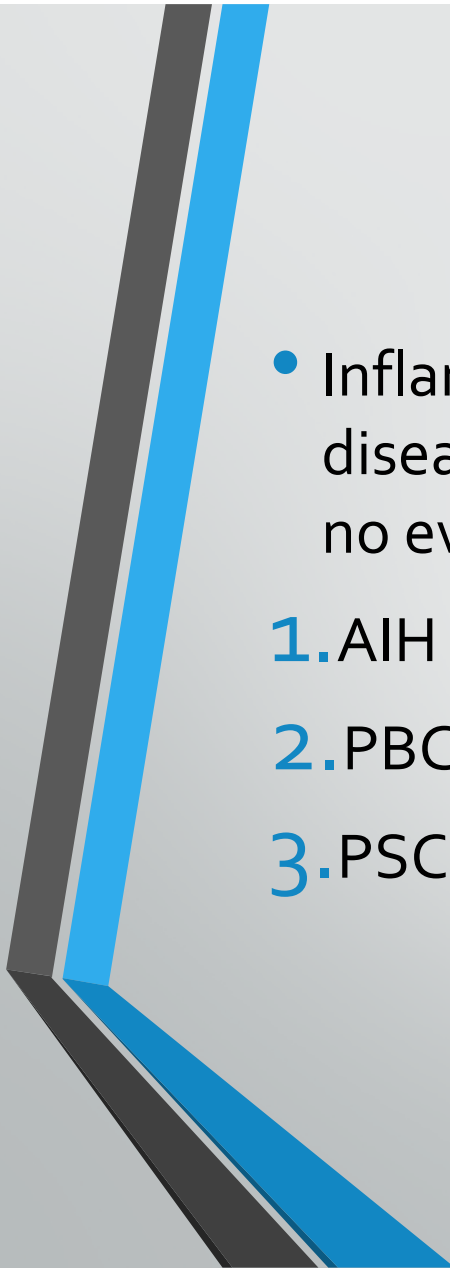


Autoimmune hepatitis, AIH

Immunopathogenesis and lab diagnosis

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- 
- Inflammatory hepatobiliary disease: chronic autoimmune disease with predominant hepatic and biliary manifestations with no evidence of infections

1. AIH

2. PBC

3. PSC

AIH

- A severe liver disease affecting all age groups worldwide with unknown etiology resulting from immune-mediated destruction of hepatocytes

Incidence

- 1:100,000, preferentially affects females
- ♂: ♀ ratio: 1:4

Immunopathogenesis

Genetics: HLA class II DRB1

HLA-DRB1* 0301, DRB1 * 0401, DRB1 * 0405, etc.

Certain HLA alleles associated with AIH clinical manifestation, response to treatment and prognosis

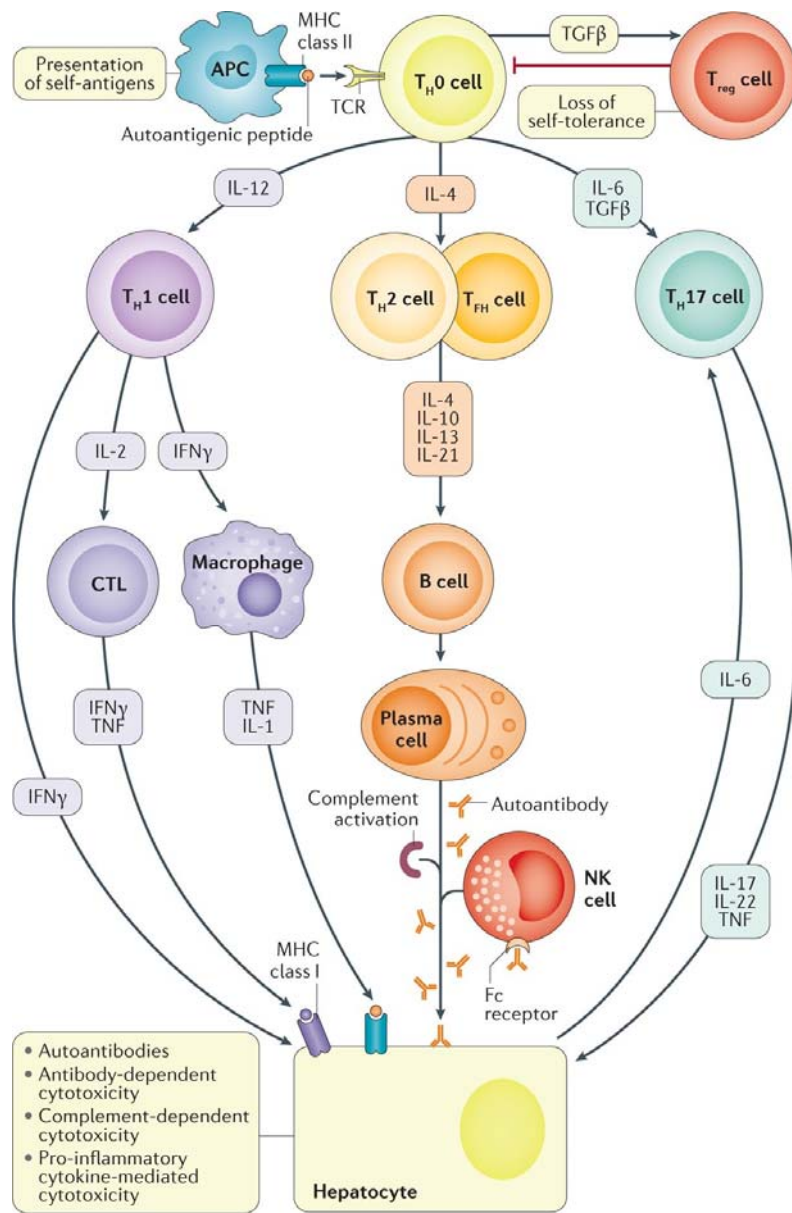
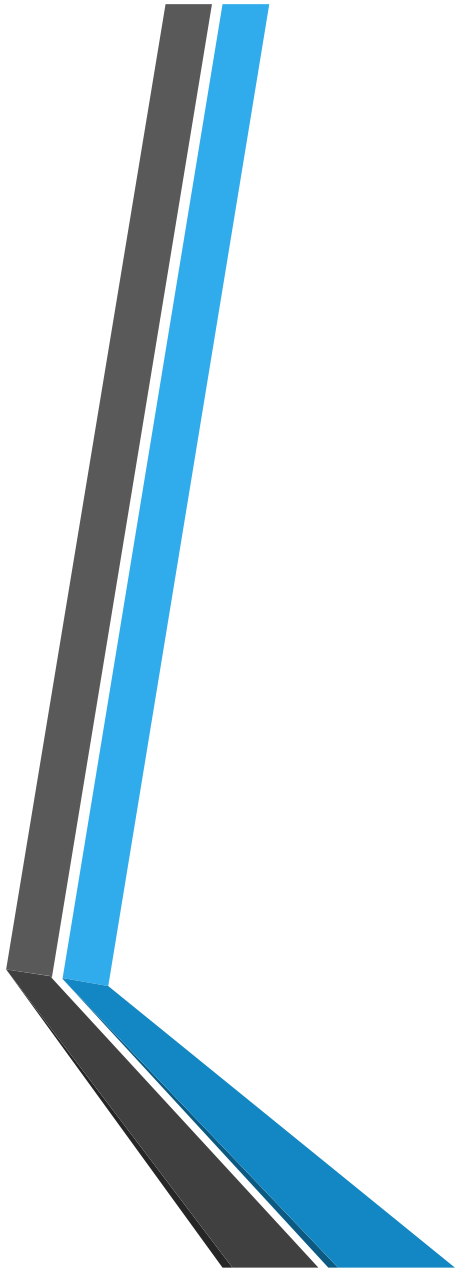
Immunopathogenesis

- Environmental factors
 1. Infections: HCV
 2. Medications: antibiotics, statins, Anti-TNF
- Drug induced AIH is slightly different from clinical AIH and usually does not require long term therapy

CD₄ + T cells

- Th₁
- Th₂
- Th₁₇

- No clear evidence to show the definite role of each Th subtypes
- As in PBC, Th₁₇ have been reported in peripheral blood and liver of patients with AIH compared with healthy controls



Diagnostic criteria

- No genetic liver disease
- No active viral infection
- No toxic or alcohol injury
- Histological findings
- Auto antibodies
- Laboratory features

Types of AIH based on antibody patterns

- Type I: ANA, ASMA: affect any age and sex, high Ig
- Type II: LKM-1, LC₁, primarily male of young age.

Chemistry

- Elevation of ALT, AST cholestatic pattern
- ALP, Bilirubin
- Serum protein- γ globulin elevation

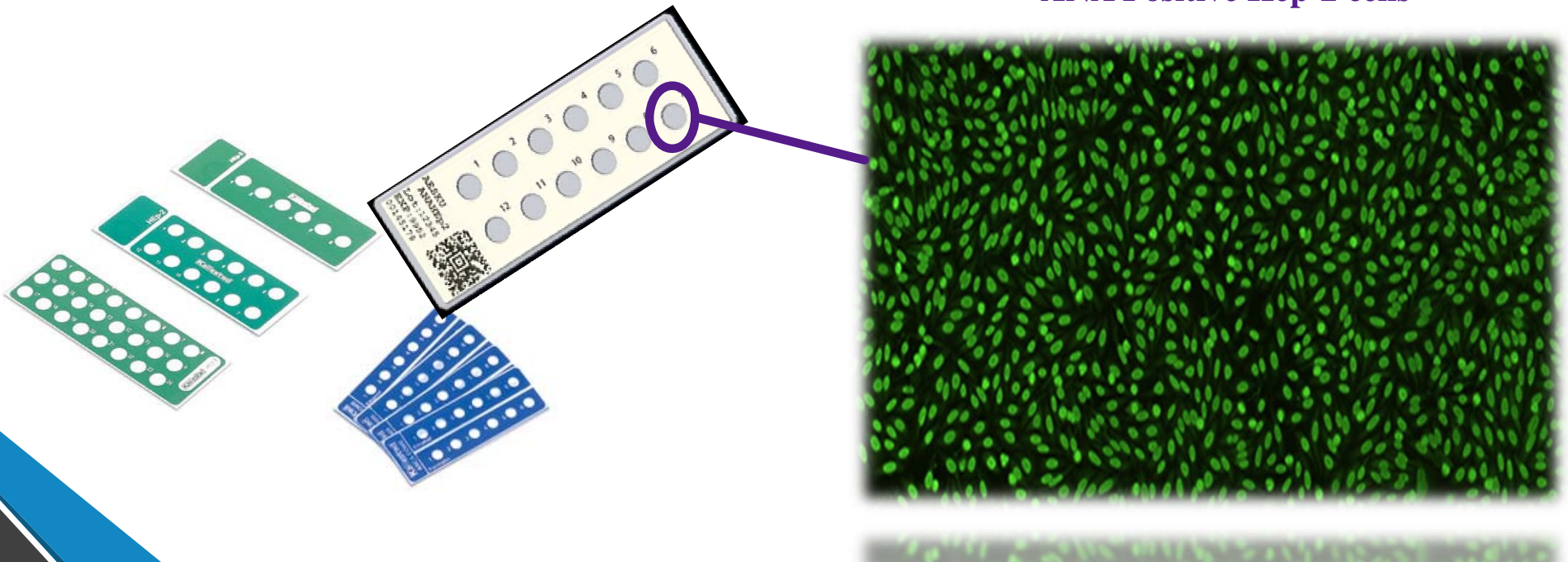
Anti Nuclear Antibodies (ANA)

- ANA test is the most commonly antibody detection test that performed in many clinical and immunology laboratories in the worldwide;
- for example, **8854** tests per year (**740** per month) are performed in Massoud Lab.
- Routinely ANA test performed in fluorescent (IFA) and Enzymatic (EIA) methods.
- Based on the confirmation of all guidelines, the gold standard method for evaluation anti-nuclear antibodies is Indirect fluorescent assay in human cell lines or animal tissues as substrate; that called FANA

Hep-2 as substrate

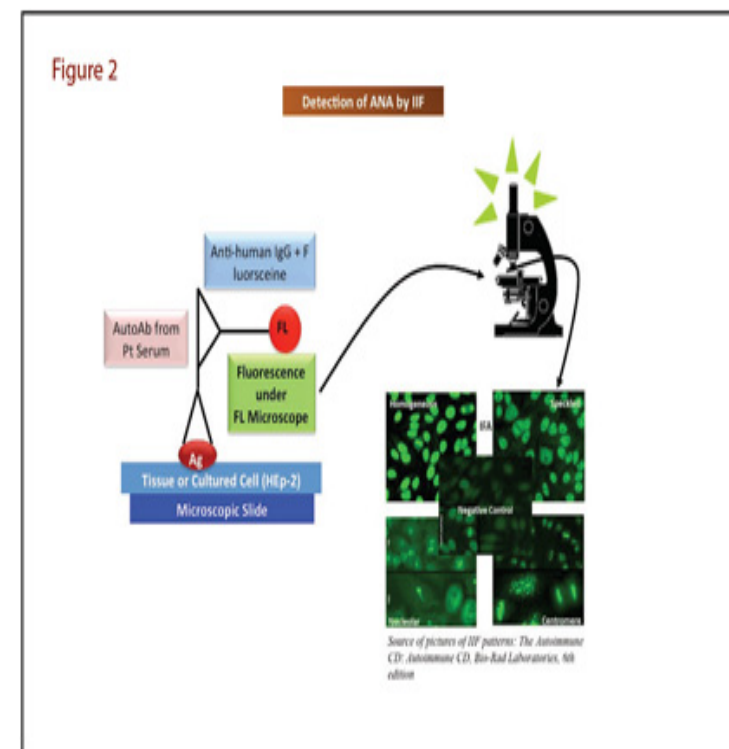
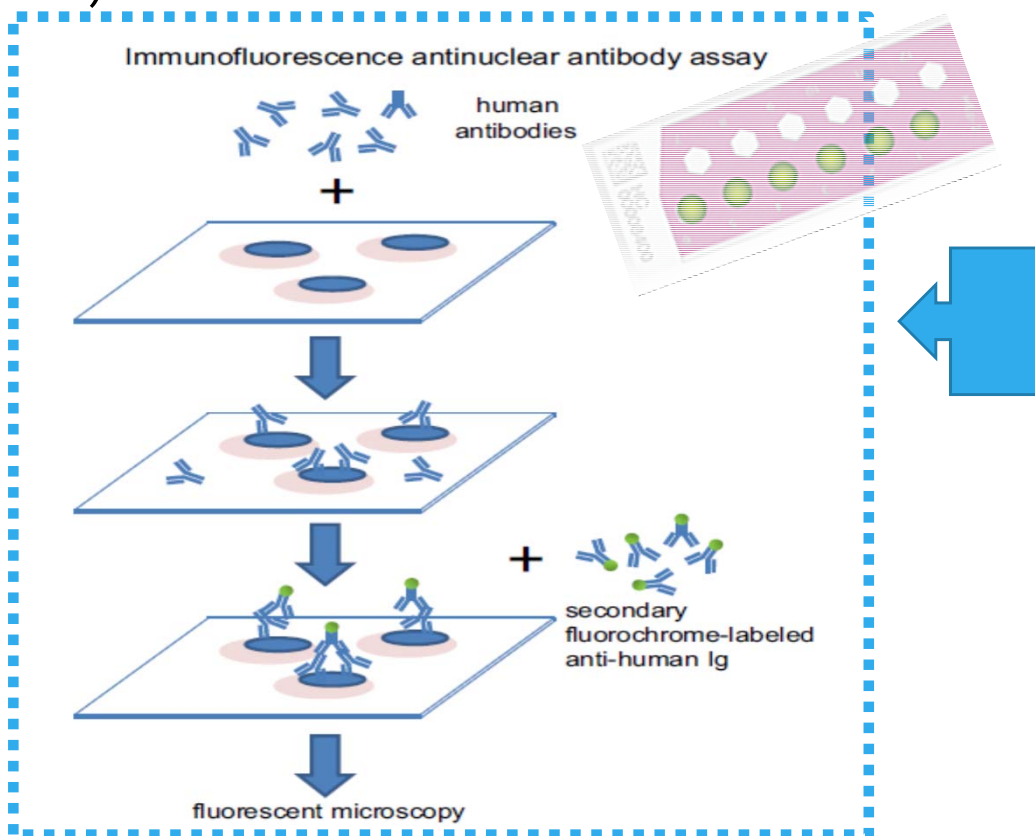
- These are obtained from cultured esophageal squamous cell carcinoma cells. The cells are available commercially, prefixed on glass slides (CCL-23, ATTC).

ANA Positive Hep-2 cells



Sample for ANA test: **blood serum**

- The common tests used for detecting and quantifying ANAs are **indirect immunofluorescence (IFA)** and enzyme-linked immunosorbent assay (**ELISA**).



Serum autoantibodies

- SMAs react with different proteins ,actin, tubulin, vimentin, desmin, cytokeratin and cytoskeletal components, microfilament, microtubule, intermediate filaments
- High titer (>1:80) is sensitive marker of AIH-1 found in up to 80% of cases
- SMA and raised ALT individuals indicate higher risk with PPV of 22%

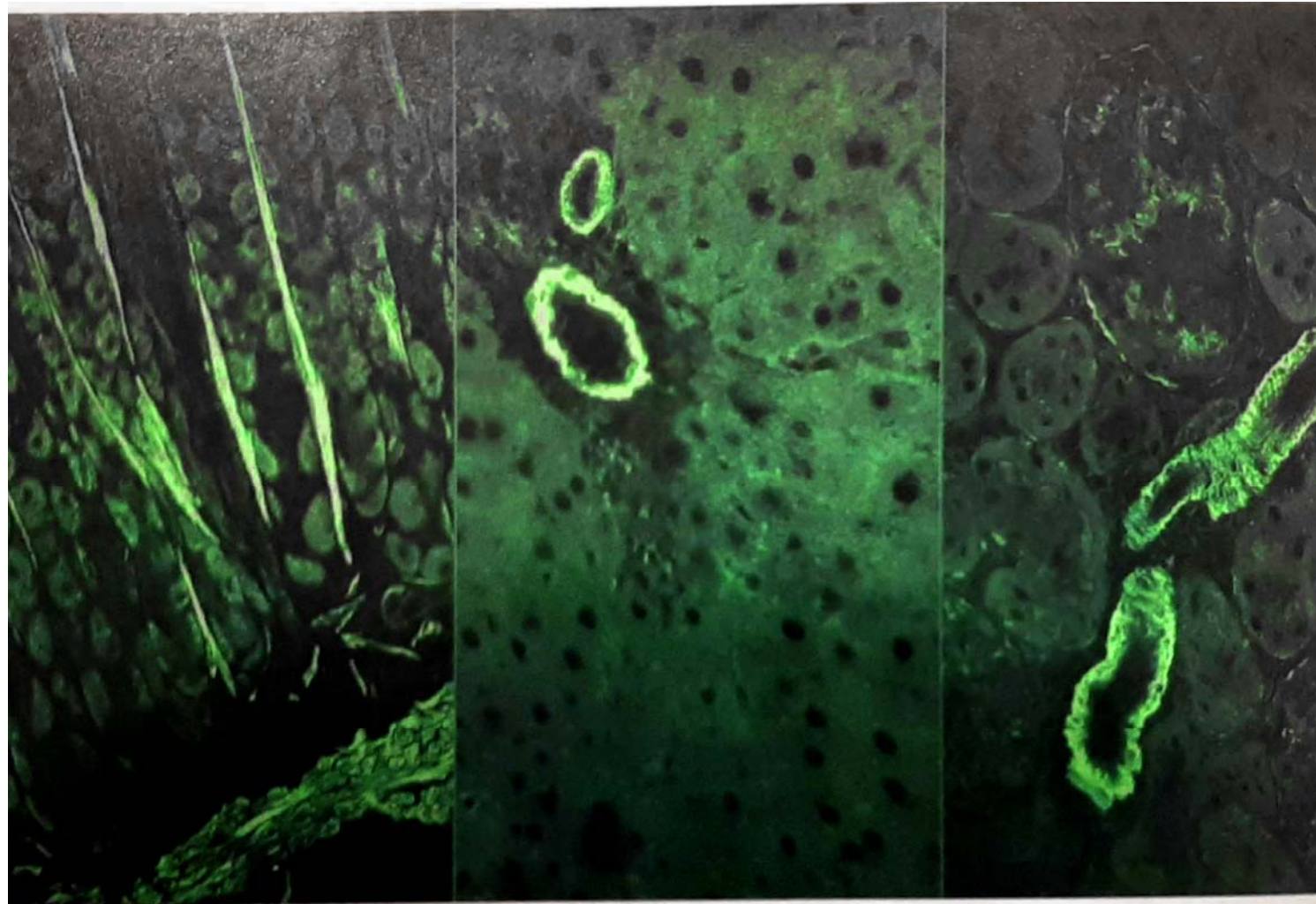


Fig. 3.4 SMA serum on rat stomach/liver/kidney

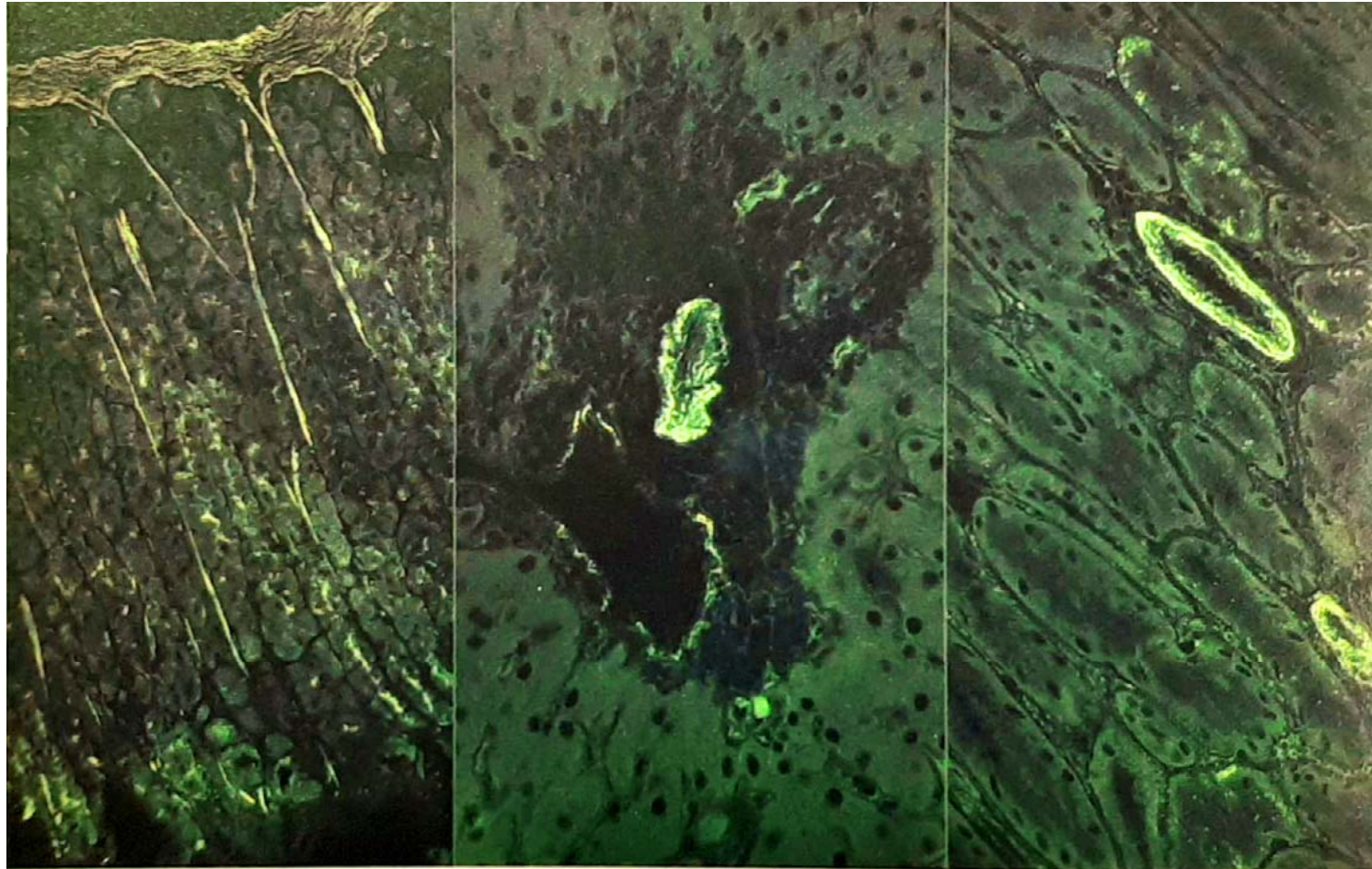


Fig. 3.5 SMA serum on monkey stomach/liver/kidney

Serum Autoantibodies

- LKM-1 (liver kidney microsomal-1)
- Main serological markers of AIH-2
- Recognize the proximal and renal tubule and hepatocellular cytoplasm.
- 50KD autoantigen cytochrome P₄₅₀ 2D6
- 316 and 327 a.a. sequence homology in AIH and HCV , a key target for autoimmunity
- Pathogenic role and prognostic significance are debated

Serum Autoantibodies

- LKM-2, LKM-3
- LKM-2 directed against Cyp2c9 found in drug induced hepatitis
- LKM-3 directed against UGT_{1A}, 10% of AIH-2 either alone or in combination with LKM-1

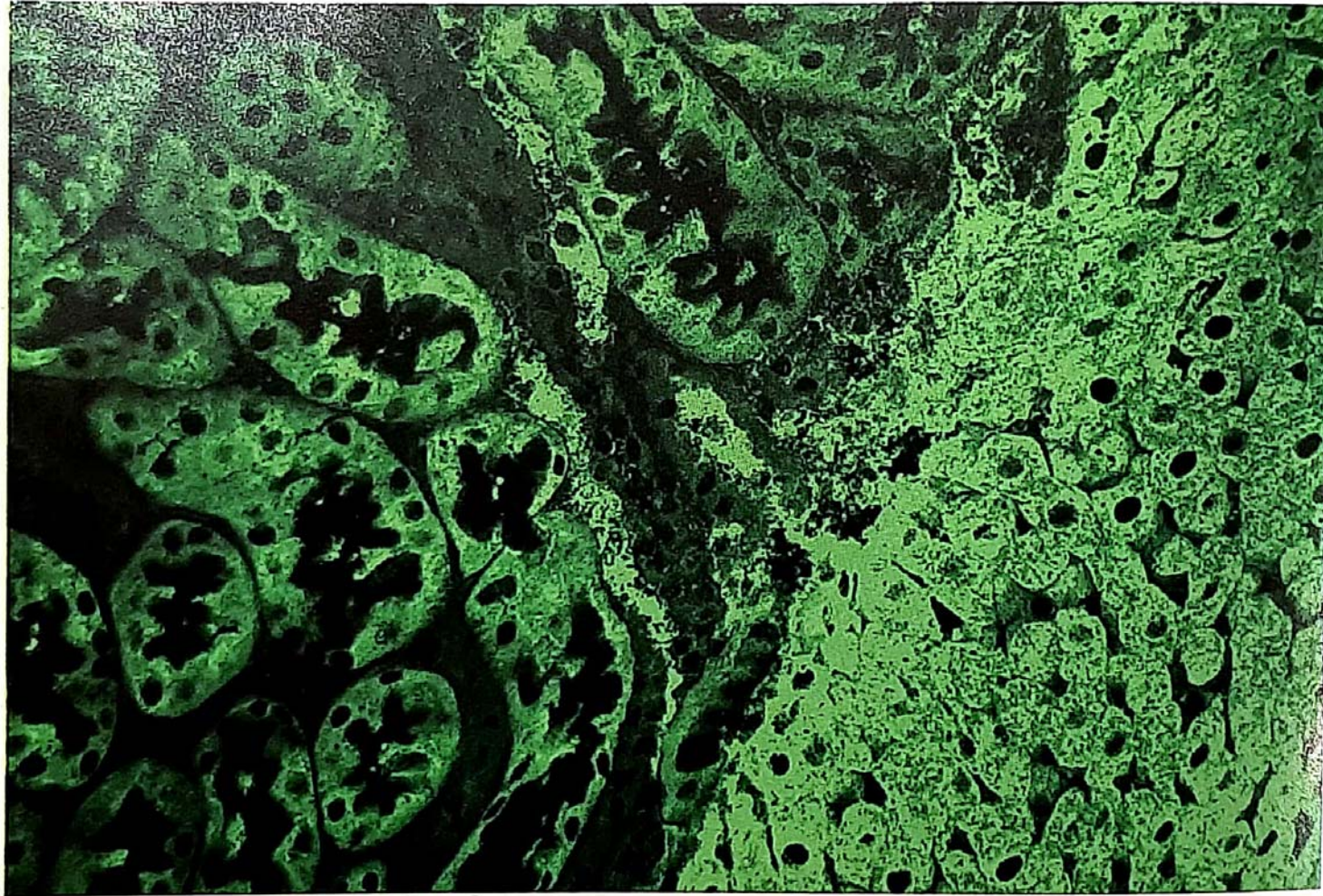


Fig. 3.8 Typical LKM-1 on rat liver and rat kidney

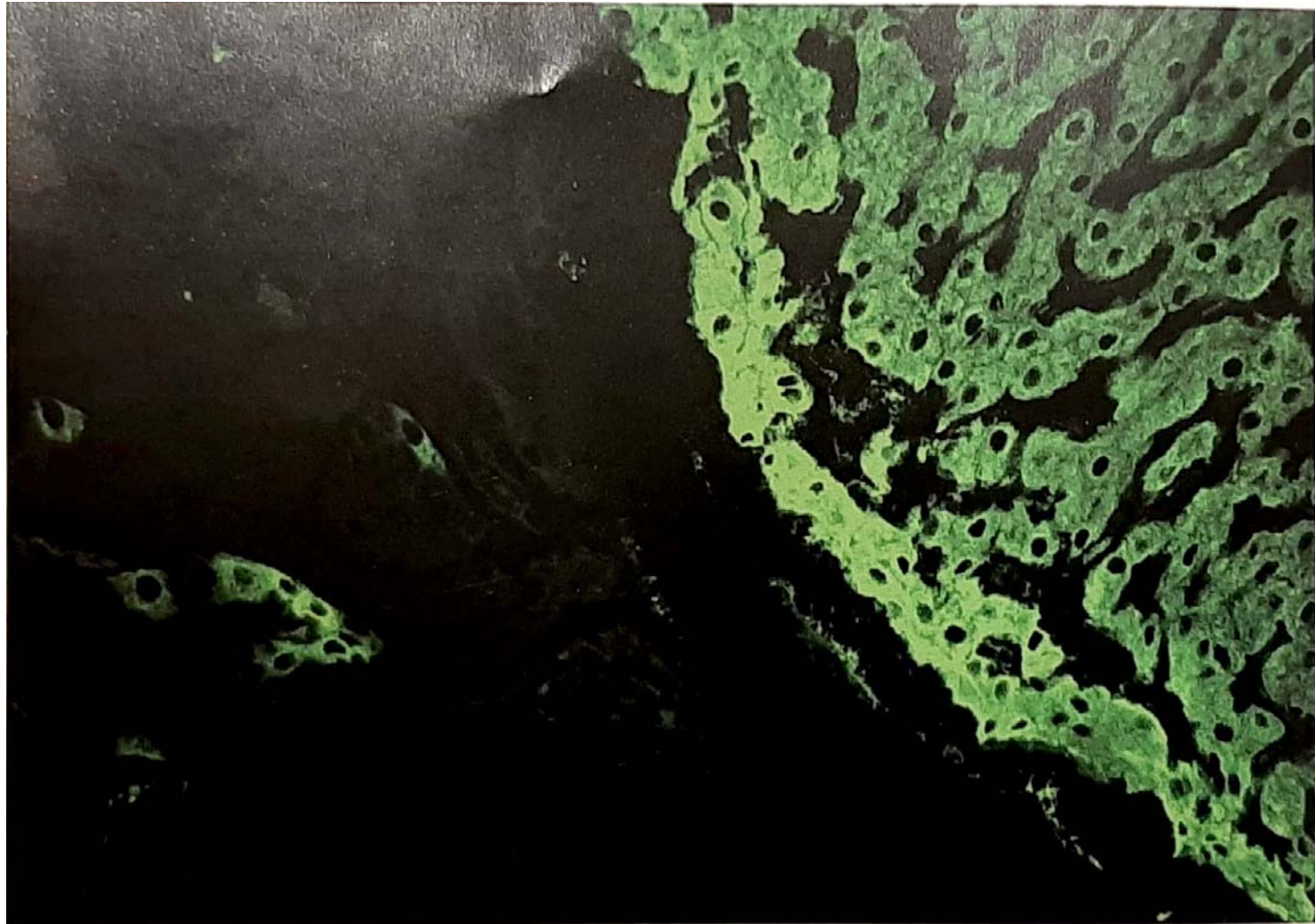


Fig. 3.7 LKM-1 staining monkey liver but monkey kidney is negative

Serum Autoantibodies

- **Anti-SLA/LP**: occasionally found in patients with AIH who are negative for ANA, SMA, LKM-1 pediatric patients with autoimmune cholangitis
- **Anti-LC1**: 50% of AIH-2 and less frequently in AIH-1 Interestingly correlate with severity and progression
- **Anti-ASGPR**: 90% of AIH coexist with other autoantibodies while lacking specifically Associate with more florid inflammation
- pANCA: AIH-1, PSC, Chronic viral hepatitis

Histology

- The role in the management of AIH remains critical, all patients should undergo liver biopsy and remains gold standard for grading, staging and response to therapy



Thanks for your attention!