Chromosome 12p abnormalities are characteristic of germ cell tumors – isochromosome 12p and 12p overrepresentation. Some can be detected by karyotyping. FISH study of 21 dysgerminomas showed chromosome 12 abnormalities in 17 (81%): 16 had i(12p) (76%) and 5 had overrepresentation of 12p. 

**Genetic Studies of Dysgerminoma**

- Chromosome 12p abnormalities are characteristic of germ cell tumors – isochromosome 12p and 12p overrepresentation.
- Some can be detected by karyotyping.
- FISH study of 21 dysgerminomas showed chromosome 12 abnormalities in 17 (81%):
  - 16 had i(12p) (76%)
  - 5 had overrepresentation of 12p.

*Mod Pathol 2006; 19:611-615*
**Dysgerminoma Immunohistochemistry**

- **Cytoplasm and membrane staining**
  - PLAP: Placental alkaline phosphatase, cross reacts with germ cell alkaline phosphatase; some carcinomas +
  - CD117 (c-kit): Membrane staining specific for dysgerminoma; other tumors, such as melanoma and GIST, show cytoplasmic staining
  - D2-40 (podoplanin): Also stains lymphovascular endothelial cells; cytoplasmic staining can be so intense that it overwhelms membrane staining

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**Molecular Abnormalities of KIT in Dysgerminoma**

- KIT gene located at chromosome 4q12
- KIT mutations in GIST are in exon 11

- Hoei-Hansen et al:
  - Point mutations in exon 17 codon 816 in 5/19 – 26%, only in unilateral tumors
  - KIT mutated in 1/5 patients with gonadoblastoma

- Cheng et al:
  - Point mutations in exon 17 codon 816 in 6/22 – 27%, only in unilateral tumors
  - Mutation correlated with advanced stage
  - KIT amplification in 6/22 – 27%; not correlated with KIT mutation
  - No KIT mutation or amplification in dysgerminoma with gonadoblastoma
  - KIT mutation not associated with chromosome 12p abnormalities

- No correlation between KIT mutation or amplification and immunostaining for CD117 (kit).

Hoei-Hansen CE et al. Mol Cancer 2007; 6:12
Cheng L et al. Cancer 2010 (epub)
Dysgerminoma Immunohistochemistry

- **Nuclear transcription factors**
  - Stem cell – primordial germ cell markers
  - Strong staining in > 90% of tumor cells
  - Three stains in use currently
    1. **OCT4**: Positive in dysgerminoma and embryonal carcinoma
    2. **NANOG**: Positive in dysgerminoma and embryonal carcinoma
    3. **SALL4**: Positive in dysgerminoma, embryonal carcinoma, and yolk sac tumor
  - **SOX2**: Negative in dysgerminoma, positive in embryonal carcinoma

<table>
<thead>
<tr>
<th>OCT4</th>
<th>NANOG</th>
<th>SALL4</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Cytokeratin minimal +, EMA -</th>
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</table>

UCSF Staining Panel for Dysgerminoma

<table>
<thead>
<tr>
<th>Stain</th>
<th>Expected Result</th>
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</thead>
<tbody>
<tr>
<td>Cytokeratin AE1/AE3</td>
<td>- Or minimal</td>
</tr>
<tr>
<td>EMA</td>
<td>-</td>
</tr>
<tr>
<td>CD117</td>
<td>+ Membranes</td>
</tr>
<tr>
<td>D2-40</td>
<td>+</td>
</tr>
<tr>
<td>OCT4</td>
<td>+</td>
</tr>
<tr>
<td>SALL4</td>
<td>+</td>
</tr>
</tbody>
</table>

Unusual Variants ➔ Diagnostic Problems

- **Stromal Changes**
  - Prominent granulomatous reaction
  - Marked fibrosis
  - Extensive Necrosis

- **Unusual architecture or cytology**
  - Tubular - alveolar dysgerminoma
  - Trabecular dysgerminoma
  - Anaplastic dysgerminoma
  - Dysgerminoma with STGC

- **Fixation artifacts**
Alveolar pattern  Trabecular pattern

HCG Highlights STGC in Dysgerminoma

Fixation Artifact
Dysgerminoma Therapy

• Surgical treatment
  – Young patients ➔ conservative treatment
  – Stage IA: USO
  – More advanced: USO, limited debulking

• Additional therapy
  – Radiotherapy
  – Chemotherapy
  – No treatment, close observation

Germ Cell Tumors
Survival Changes – SEER Data – All Stages

<table>
<thead>
<tr>
<th>Type</th>
<th>1973-1977 %</th>
<th>1998-2002 %</th>
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<tbody>
<tr>
<td>Dysgerminoma</td>
<td>83.5</td>
<td>96.9</td>
</tr>
</tbody>
</table>

Obstet Gynecol 2006;107:1075-1085

Dysgerminoma Histogenesis

Hoei-Hansen CE et al. Mol Cancer 2007; 6:12
Dysgerminoma

Differential Diagnosis

- Embryonal carcinoma
- Yolk sac tumor
- Large cell lymphoma
- Metastatic melanoma
- Clear cell carcinoma
- Mixed germ cell tumor

Embryonal Carcinoma

Yolk Sac Tumor

Case 14 Clinical History

Composite Case

- TR64-13818 The patient was a 16 year old female. Four weeks prior to admission she developed abdominal pain and rebound tenderness, suggestive of peritonitis. She had a mild fever. Antibiotics were administered and the discomfort slowly diminished and the temperature returned to normal. There was a suggestion of enlargement of the right ovary. She was seen 3 weeks later at which time a large mass extending almost to the umbilicus was palpated. The patient was taken to surgery and a large mass of the left ovary was found.
- TR90-26689 The patient was a 30 year old woman who presented with a 1-week history of pelvic pain. At surgery, a large right ovarian tumor was found and removed.