

**MINI-REVIEW**

NEWS BULLETIN FOR AXIS-SHIELD DENSITY GRADIENT MEDIA

SUBCELLULAR MEMBRANE ANALYSIS OF TUMOR CELLS USING OPTIPREP™

- OptiPrep™ is a sterile 60% (w/v) solution of iodixanol, density = 1.32 g/ml
- Some of the principal applications of OptiPrep™ are concerned with the resolution of subcellular membranes and since OptiPrep™ was introduced in 1994 over one and a half thousand papers have been published that report the use of this density gradient medium.
- This Mini-Review principally provides (in Section 2) a bibliography of all those papers reporting the use of OptiPrep™ in the analysis of subcellular membranes from tumors and tumor cell cultures. Section 1 briefly summarizes the advantages of using OptiPrep™ and the technical data that is available from Axis-Shield.

1. Technical background to the use of OptiPrep™**1a. Gradient preparation and properties**

There are many advantages to the use of iodixanol gradients compared to those of sucrose or Percoll®.

1. Gradient solutions are prepared directly by simple dilution of OptiPrep™ with the homogenization medium: if the homogenization medium is isoosmotic all of the gradient solutions will be isoosmotic.
2. Before preparing isoosmotic gradient solutions from Percoll®, it must be diluted with 0.1 vol. of 2.5M sucrose: 2.5M sucrose is difficult to prepare and measure accurately.
3. All sucrose gradients are hyperosmotic.
4. Although both iodixanol and Percoll® form self-generated gradients, only those of iodixanol are useful at the g-force required to band the membrane vesicles of a microsome fraction.

1b. Applications

1. Iodixanol gradients allow isolation of nuclei by buoyant density banding in isoosmotic gradients in 20 min at 10,000 g. In hyperosmotic sucrose gradients, nuclei are too dense to band isopycnicly and require 1-2 h at 100,000 g to pellet.
2. Mitochondria, peroxisomes and lysosomes can be purified in discontinuous, continuous or self-generated iodixanol gradients.
3. Membrane trafficking, cell signaling, endocytosis and exocytosis have been analyzed under a variety of gradient conditions. Separations have been carried out on the basis of buoyant density or sedimentation velocity, in continuous, discontinuous or self-generated iodixanol gradients; bottom- or top-loaded with centrifugation times of 1-18 h. Gradients need to be tailored to specific requirements. For example two layer discontinuous gradients are sufficient for bulk isolation of lipid rafts but analysis of subdomains of rafts requires either multi-layer discontinuous or continuous gradients. *Cis-medial* Golgi separation from TGN may best be achieved in sedimentation velocity gradients and these gradients also seem very effective in separations of early endosomes from both apical and basolateral plasma membrane domains.
4. Detailed protocols for the isolation of all subcellular membranes may be accessed from the Index of the "Subcellular membranes" file either on the Axis-Shield Applications CD or from the following Axis-Shield website: www.axis-shield-density-gradient-media.com.

1c. Analysis of gradients

Most analysis of subcellular membrane density gradients is achieved by a combination of SDS-PAGE and electroblotting with antibodies. Iodixanol does not interfere with either process; if it is necessary to concentrate the gradient fractions, TCA precipitation of the protein is recommended. Iodixanol is soluble in acid solutions, but not acetone. Percoll® on the other hand must be removed prior to SDS-PAGE because it causes irregular protein banding in the gel. Removal of iodixanol prior to membrane analysis is only an absolute requirement for electron microscopy.

2. Bibliography

2a Reference list

The references are listed chronologically below.

- Section 2b lists all of the tumor cell types whose subcellular membranes have been purified in iodixanol gradients; the numbers against each entry indicate the relevant reference numbers from Section 2a
 - Section 2c list all the subcellular membranes and/or the molecule or function studied; the numbers against each entry indicate the relevant reference numbers from Section 2a
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2b. Tumor cell types

Adenocarcinoma cells: 4, 8
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2c. Subcellular membrane, molecule, function

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- Tumor necrosis factors: 28
- Tyrosinase: 4

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Excellence in Separations

DENSITY GRADIENT MEDIA

A photograph of two test tubes containing density gradient media. The left tube shows a dark liquid, and the right tube shows a lighter liquid. Chemical structures are overlaid on the image, including a benzene ring with iodine atoms and a side chain with a methyl group, a carbonyl group, and a hydroxyl group. A vertical scale on the left side of the image shows numbers 20, 30, and 40.

Axis-Shield has the solutions

The logo for Axis-Shield, featuring a stylized figure holding a shield and a sword, with the text 'AXIS-SHIELD' below it.

ISO 9001 and ISO 13485 Certified



Certificate No. 255