Cultivated Meat: Safety & Regulatory Challenges for Cultivated Meat

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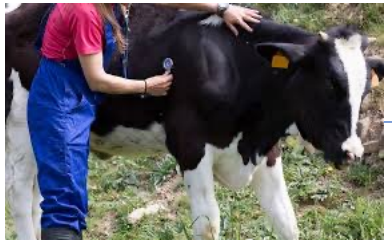
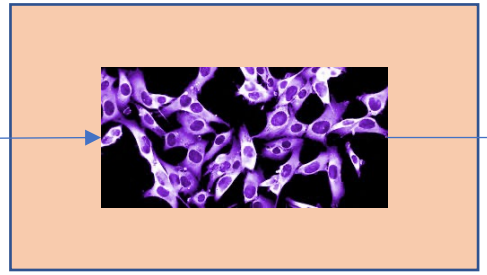
Basics of Cultivated Meat Production

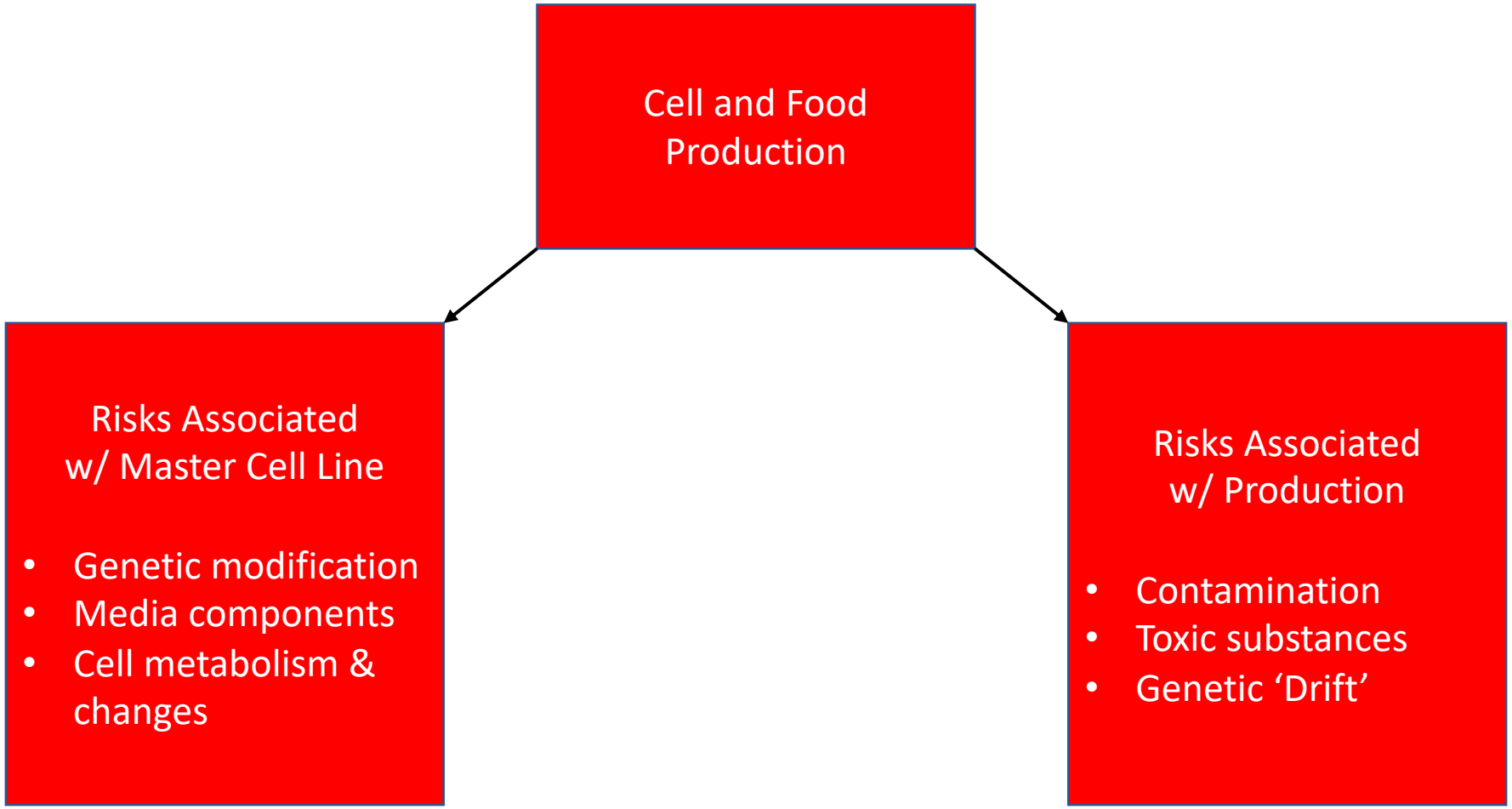






- Specific processes developed for both unstructured and structured meat make each biomanufacturing process unique (i.e., impact of media, cell types and process engineering)

Risk Types for Cell Based Food Production



Master Cell Line Creation

Use of genetic tools or cell adaptation to:

- Turn off specific genes
- Turn on specific genes
- Insertion of additional copies of endogenous genes
- Insertion of additional copies of endogenous genes

Safety Concerns:

- Changes to DNA in mammalian cells can be transferred to those ingesting modified animal cells
- Proteins may be modified to become allergenic to humans

Reality:

- There is no data that suggests ingestion of modified animal DNA can transfect into human genome
- Allergenicity testing against known allergen sequences is required as part of safety assessment

Food Safety Risks and Benefits of Production

Process Step	Risks	Benefits
Source animal and tissue harvest	Sample infection and contamination	Small biopsy from healthy animal with minimal discomfort
Cell isolation	Sample contamination during initial handling	Sterile environment needed for adequate cell growth
Cell Line Creation	- Integration of viral, bacterial or other exogenous DNA - Contamination (incl. protein)	Strict Control over modifications of genome and characterization of cells
Master Cell Bank (MCB) & Working Cell Bank (WCB) creation	- Contamination - Genetic drift	Creation of a single source of cells for manufacturing
Biomanufacturing (biomass production)	- Microbial or particulate contamination - Toxic substances	Sterile environment prevents typical food borne microbial and contamination issues
Harvesting & Product Manufacturing	Same as for traditional food production	Same as for traditional food production
Overall	Contamination of biomass	Sterile controlled production

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Risks Mitigation steps related to production

Safety Management Steps	Risks	Benefits
Good Cell Culture Practices & Good Manufacturing Practices	Contamination and control	Reduces likelihood of processes errors impacting safety of production
HACCP and Food Safety Plan	Contamination and out of spec product	Reduces possibility that contaminated or poor-quality product is released
Material Management System	Use of non suitable ingredients and starting materials	Quality control from the initial stages of manufacturing
Vendor Qualification Program	Use of materials outside of specifications	Assurance of stable and certifiable supply of materials of high standard
Microbiological Testing	Presence of adventitious agents	Demonstration of lack of hazardous contamination by infectious agents
Biochemical Analysis of product	Generation of toxic byproducts or metabolites	Ensures process is as expected and within nominal ranges for unexpected chemicals
Residue testing	Presence of toxic carry over components	Check on final product to ensure compliance with exisiting safety standards

Regulatory Landscape

Global Regulatory Activity

Many national regulatory authorities are already engaged with companies:
The question of GM status is country by country assessment

Country	Regulatory Status
Singapore	- First approval of cell-based chicken nugget - Supportive gov't climate (i.e. FRESH) - Evolving knowledge base for regulators
Israel	- Supportive gov't, unclear regulatory pathway
China	- Suggested that existing GM regulations can be utilized - Complex regulatory environment
Australia/NZ	- Authorities state Novel Foods regulations can support - GM issue may apply as well
Japan	- Regulatory process in development, novel foods do not require premarket approval but the path for novel foods is unclear
EU	- Novel Food regulations in place, very conservative safety assessment approach complicates approval estimates

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US Regulatory Environment

2019 - Joint agreement between FDA and USDA to co-regulate meat and poultry products

FDA

- would be responsible for the safety assessment of the Master Cell line and the production process including media components
- FDA would be responsible for all seafood and non livestock animal labeling and nutrition requirements
    - Excluding catfish

USDA

- would be responsible for the approval of labeling and nutrition standards for all live - stock animals (i.e., poultry, beef, pork)

Transition from FDA to USDA Oversight:

At time of cell harvest (unique to each process)

Co-ownership of site inspections and approvals

- USDA requiring on site, daily inspections and certification of batches

Essential Components of US Safety Assessment

Master Cell line characterization

- Genetic sequence
- Identification of all intended genetic manipulations
- Identification of unintended genetic impacts
- Presence of any adventitious agents
  - Bacterial
  - Viral
  - Fungal
- Presence of allergenic proteins

Essential Components of US Safety Assessment (con't)

Media Characterization

- Amino Acids
- Growth Factors
- Proteins (i.e. albumin)
- Fetal Bovine Serum
- Salts
- Nutrients
- Buffers

Process Conditions

- Equipment used
- Time and temperature specific
- Starting conditions for media
- Seeding requirements
- Growth rates
- Media replacement scheme
- Metabolite profile
  - Disappearance of media components
  - Presence of metabolites

In summary: Mammalian cells are not inherently dangerous to consume

- The approach we have seen from the regulators is to focus on the changes made to the primary cells collected in biopsy
    - Less concerned about endogenous genetic manipulations (i.e. sequence deletions, adding extra copies of genes or promotors)
    - More interested if exogenous genes are added to the primary cell DNA
    - Components from media and cell replication (i.e., metabolites) that remain in food are a major concern
- Scientifically, there is no reason to believe that genetic manipulations are in and of themselves dangerous

Ignorance and misinformation are our biggest challenge!

Mistrust in science and government authorities weigh heavily on consumer perceptions of new technology

Misinformation by poorly trained and educated social media ”experts” is overwhelming the science-based sources of information

Corporate competition also results in a significant amount of misinformation and consumer mistrust

QUESTIONS?

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