

MEDICINA:

Ciências da saúde e pesquisa interdisciplinar



*Benedito Rodrigues da Silva Neto
(Organizador)*

 **Atena**
Editora
Ano 2021

MEDICINA:

Ciências da saúde e pesquisa interdisciplinar



3

Benedito Rodrigues da Silva Neto
(Organizador)

 **Atena**
Editora
Ano 2021

Editora chefe

Profª Drª Antonella Carvalho de Oliveira

Assistentes editoriais

Natalia Oliveira

Flávia Roberta Barão

Bibliotecária

Janaina Ramos

Projeto gráfico

Natália Sandrini de Azevedo

Camila Alves de Cremo

Luiza Alves Batista

Maria Alice Pinheiro

Imagens da capa

iStock

Edição de arte

Luiza Alves Batista

Revisão

Os autores

2021 by Atena Editora

Copyright © Atena Editora

Copyright do Texto © 2021 Os autores

Copyright da Edição © 2021 Atena Editora

Direitos para esta edição cedidos à Atena Editora pelos autores.

Open access publication by Atena Editora



Todo o conteúdo deste livro está licenciado sob uma Licença de Atribuição Creative Commons. Atribuição-Não-Comercial-NãoDerivativos 4.0 Internacional (CC BY-NC-ND 4.0).

O conteúdo dos artigos e seus dados em sua forma, correção e confiabilidade são de responsabilidade exclusiva dos autores, inclusive não representam necessariamente a posição oficial da Atena Editora. Permitido o *download* da obra e o compartilhamento desde que sejam atribuídos créditos aos autores, mas sem a possibilidade de alterá-la de nenhuma forma ou utilizá-la para fins comerciais.

Todos os manuscritos foram previamente submetidos à avaliação cega pelos pares, membros do Conselho Editorial desta Editora, tendo sido aprovados para a publicação com base em critérios de neutralidade e imparcialidade acadêmica.

A Atena Editora é comprometida em garantir a integridade editorial em todas as etapas do processo de publicação, evitando plágio, dados ou resultados fraudulentos e impedindo que interesses financeiros comprometam os padrões éticos da publicação. Situações suspeitas de má conduta científica serão investigadas sob o mais alto padrão de rigor acadêmico e ético.

Conselho Editorial

Ciências Humanas e Sociais Aplicadas

Prof. Dr. Alexandre Jose Schumacher – Instituto Federal de Educação, Ciência e Tecnologia do Paraná

Prof. Dr. Américo Junior Nunes da Silva – Universidade do Estado da Bahia

Profª Drª Andréa Cristina Marques de Araújo – Universidade Fernando Pessoa

Prof. Dr. Antonio Carlos Frasson – Universidade Tecnológica Federal do Paraná

Prof. Dr. Antonio Gasparetto Júnior – Instituto Federal do Sudeste de Minas Gerais

Prof. Dr. Antonio Isidro-Filho – Universidade de Brasília

Prof. Dr. Arnaldo Oliveira Souza Júnior – Universidade Federal do Piauí
Prof. Dr. Carlos Antonio de Souza Moraes – Universidade Federal Fluminense
Prof. Dr. Crisóstomo Lima do Nascimento – Universidade Federal Fluminense
Prof^a Dr^a Cristina Gaio – Universidade de Lisboa
Prof. Dr. Daniel Richard Sant’Ana – Universidade de Brasília
Prof. Dr. Deyvison de Lima Oliveira – Universidade Federal de Rondônia
Prof^a Dr^a Dilma Antunes Silva – Universidade Federal de São Paulo
Prof. Dr. Edvaldo Antunes de Farias – Universidade Estácio de Sá
Prof. Dr. Elson Ferreira Costa – Universidade do Estado do Pará
Prof. Dr. Eloi Martins Senhora – Universidade Federal de Roraima
Prof. Dr. Gustavo Henrique Cepolini Ferreira – Universidade Estadual de Montes Claros
Prof. Dr. Humberto Costa – Universidade Federal do Paraná
Prof^a Dr^a Ivone Goulart Lopes – Istituto Internazionele delle Figlie de Maria Ausiliatrice
Prof. Dr. Jadson Correia de Oliveira – Universidade Católica do Salvador
Prof. Dr. José Luis Montesillo-Cedillo – Universidad Autónoma del Estado de México
Prof. Dr. Julio Candido de Meirelles Junior – Universidade Federal Fluminense
Prof^a Dr^a Lina Maria Gonçalves – Universidade Federal do Tocantins
Prof. Dr. Luis Ricardo Fernandes da Costa – Universidade Estadual de Montes Claros
Prof^a Dr^a Natiéli Piovesan – Instituto Federal do Rio Grande do Norte
Prof. Dr. Marcelo Pereira da Silva – Pontifícia Universidade Católica de Campinas
Prof^a Dr^a Maria Luzia da Silva Santana – Universidade Federal de Mato Grosso do Sul
Prof. Dr. Miguel Rodrigues Netto – Universidade do Estado de Mato Grosso
Prof. Dr. Pablo Ricardo de Lima Falcão – Universidade de Pernambuco
Prof^a Dr^a Paola Andressa Scortegagna – Universidade Estadual de Ponta Grossa
Prof^a Dr^a Rita de Cássia da Silva Oliveira – Universidade Estadual de Ponta Grossa
Prof. Dr. Rui Maia Diamantino – Universidade Salvador
Prof. Dr. Saulo Cerqueira de Aguiar Soares – Universidade Federal do Piauí
Prof. Dr. Urandi João Rodrigues Junior – Universidade Federal do Oeste do Pará
Prof^a Dr^a Vanessa Bordin Viera – Universidade Federal de Campina Grande
Prof^a Dr^a Vanessa Ribeiro Simon Cavalcanti – Universidade Católica do Salvador
Prof. Dr. William Cleber Domingues Silva – Universidade Federal Rural do Rio de Janeiro
Prof. Dr. Willian Douglas Guilherme – Universidade Federal do Tocantins

Ciências Agrárias e Multidisciplinar

Prof. Dr. Alexandre Igor Azevedo Pereira – Instituto Federal Goiano
Prof. Dr. Arinaldo Pereira da Silva – Universidade Federal do Sul e Sudeste do Pará
Prof. Dr. Antonio Pasqualetto – Pontifícia Universidade Católica de Goiás
Prof^a Dr^a Carla Cristina Bauermann Brasil – Universidade Federal de Santa Maria
Prof. Dr. Cleberton Correia Santos – Universidade Federal da Grande Dourados
Prof^a Dr^a Diocléa Almeida Seabra Silva – Universidade Federal Rural da Amazônia
Prof. Dr. Écio Souza Diniz – Universidade Federal de Viçosa
Prof. Dr. Fábio Steiner – Universidade Estadual de Mato Grosso do Sul
Prof. Dr. Fágner Cavalcante Patrocínio dos Santos – Universidade Federal do Ceará
Prof^a Dr^a Girlene Santos de Souza – Universidade Federal do Recôncavo da Bahia
Prof. Dr. Jael Soares Batista – Universidade Federal Rural do Semi-Árido
Prof. Dr. Jayme Augusto Peres – Universidade Estadual do Centro-Oeste
Prof. Dr. Júlio César Ribeiro – Universidade Federal Rural do Rio de Janeiro
Prof^a Dr^a Lina Raquel Santos Araújo – Universidade Estadual do Ceará
Prof. Dr. Pedro Manuel Villa – Universidade Federal de Viçosa
Prof^a Dr^a Raissa Rachel Salustriano da Silva Matos – Universidade Federal do Maranhão
Prof. Dr. Ronilson Freitas de Souza – Universidade do Estado do Pará
Prof^a Dr^a Talita de Santos Matos – Universidade Federal Rural do Rio de Janeiro

Prof. Dr. Tiago da Silva Teófilo – Universidade Federal Rural do Semi-Árido
Prof. Dr. Valdemar Antonio Paffaro Junior – Universidade Federal de Alfenas

Ciências Biológicas e da Saúde

Prof. Dr. André Ribeiro da Silva – Universidade de Brasília
Profª Drª Anelise Levay Murari – Universidade Federal de Pelotas
Prof. Dr. Benedito Rodrigues da Silva Neto – Universidade Federal de Goiás
Profª Drª Daniela Reis Joaquim de Freitas – Universidade Federal do Piauí
Profª Drª Débora Luana Ribeiro Pessoa – Universidade Federal do Maranhão
Prof. Dr. Douglas Siqueira de Almeida Chaves – Universidade Federal Rural do Rio de Janeiro
Prof. Dr. Edson da Silva – Universidade Federal dos Vales do Jequitinhonha e Mucuri
Profª Drª Elizabeth Cordeiro Fernandes – Faculdade Integrada Medicina
Profª Drª Eleuza Rodrigues Machado – Faculdade Anhanguera de Brasília
Profª Drª Elane Schwinden Prudêncio – Universidade Federal de Santa Catarina
Profª Drª Eysler Gonçalves Maia Brasil – Universidade da Integração Internacional da Lusofonia Afro-Brasileira
Prof. Dr. Ferlando Lima Santos – Universidade Federal do Recôncavo da Bahia
Profª Drª Fernanda Miguel de Andrade – Universidade Federal de Pernambuco
Prof. Dr. Fernando Mendes – Instituto Politécnico de Coimbra – Escola Superior de Saúde de Coimbra
Profª Drª Gabriela Vieira do Amaral – Universidade de Vassouras
Prof. Dr. Gianfábio Pimentel Franco – Universidade Federal de Santa Maria
Prof. Dr. Helio Franklin Rodrigues de Almeida – Universidade Federal de Rondônia
Profª Drª Iara Lúcia Tescarollo – Universidade São Francisco
Prof. Dr. Igor Luiz Vieira de Lima Santos – Universidade Federal de Campina Grande
Prof. Dr. Jefferson Thiago Souza – Universidade Estadual do Ceará
Prof. Dr. Jesus Rodrigues Lemos – Universidade Federal do Piauí
Prof. Dr. Jônatas de França Barros – Universidade Federal do Rio Grande do Norte
Prof. Dr. José Max Barbosa de Oliveira Junior – Universidade Federal do Oeste do Pará
Prof. Dr. Luís Paulo Souza e Souza – Universidade Federal do Amazonas
Profª Drª Magnólia de Araújo Campos – Universidade Federal de Campina Grande
Prof. Dr. Marcus Fernando da Silva Praxedes – Universidade Federal do Recôncavo da Bahia
Profª Drª Maria Tatiane Gonçalves Sá – Universidade do Estado do Pará
Profª Drª Mylena Andréa Oliveira Torres – Universidade Ceuma
Profª Drª Natiéli Piovesan – Instituto Federaci do Rio Grande do Norte
Prof. Dr. Paulo Inada – Universidade Estadual de Maringá
Prof. Dr. Rafael Henrique Silva – Hospital Universitário da Universidade Federal da Grande Dourados
Profª Drª Regiane Luz Carvalho – Centro Universitário das Faculdades Associadas de Ensino
Profª Drª Renata Mendes de Freitas – Universidade Federal de Juiz de Fora
Profª Drª Vanessa da Fontoura Custódio Monteiro – Universidade do Vale do Sapucaí
Profª Drª Vanessa Lima Gonçalves – Universidade Estadual de Ponta Grossa
Profª Drª Vanessa Bordin Viera – Universidade Federal de Campina Grande
Profª Drª Welma Emidio da Silva – Universidade Federal Rural de Pernambuco

Ciências Exatas e da Terra e Engenharias

Prof. Dr. Adélio Alcino Sampaio Castro Machado – Universidade do Porto
Profª Drª Ana Grasielle Dionísio Corrêa – Universidade Presbiteriana Mackenzie
Prof. Dr. Carlos Eduardo Sanches de Andrade – Universidade Federal de Goiás
Profª Drª Carmen Lúcia Voigt – Universidade Norte do Paraná
Prof. Dr. Cleiseano Emanuel da Silva Paniagua – Instituto Federal de Educação, Ciência e Tecnologia de Goiás
Prof. Dr. Douglas Gonçalves da Silva – Universidade Estadual do Sudoeste da Bahia
Prof. Dr. Eloi Rufato Junior – Universidade Tecnológica Federal do Paraná
Profª Drª Érica de Melo Azevedo – Instituto Federal do Rio de Janeiro

Prof. Dr. Fabrício Menezes Ramos – Instituto Federal do Pará
Profª Dra. Jéssica Verger Nardeli – Universidade Estadual Paulista Júlio de Mesquita Filho
Prof. Dr. Juliano Carlo Rufino de Freitas – Universidade Federal de Campina Grande
Profª Drª Luciana do Nascimento Mendes – Instituto Federal de Educação, Ciência e Tecnologia do Rio Grande do Norte
Prof. Dr. Marcelo Marques – Universidade Estadual de Maringá
Prof. Dr. Marco Aurélio Kistemann Junior – Universidade Federal de Juiz de Fora
Profª Drª Neiva Maria de Almeida – Universidade Federal da Paraíba
Profª Drª Natiéli Piovesan – Instituto Federal do Rio Grande do Norte
Profª Drª Priscila Tessmer Scaglioni – Universidade Federal de Pelotas
Prof. Dr. Sidney Gonçalo de Lima – Universidade Federal do Piauí
Prof. Dr. Takeshy Tachizawa – Faculdade de Campo Limpo Paulista

Linguística, Letras e Artes

Profª Drª Adriana Demite Stephani – Universidade Federal do Tocantins
Profª Drª Angeli Rose do Nascimento – Universidade Federal do Estado do Rio de Janeiro
Profª Drª Carolina Fernandes da Silva Mandaji – Universidade Tecnológica Federal do Paraná
Profª Drª Denise Rocha – Universidade Federal do Ceará
Profª Drª Edna Alencar da Silva Rivera – Instituto Federal de São Paulo
Profª Drª Fernanda Tonelli – Instituto Federal de São Paulo,
Prof. Dr. Fabiano Tadeu Grazioli – Universidade Regional Integrada do Alto Uruguai e das Missões
Prof. Dr. Gilmei Fleck – Universidade Estadual do Oeste do Paraná
Profª Drª Keyla Christina Almeida Portela – Instituto Federal de Educação, Ciência e Tecnologia do Paraná
Profª Drª Miranilde Oliveira Neves – Instituto de Educação, Ciência e Tecnologia do Pará
Profª Drª Sandra Regina Gardacho Pietrobon – Universidade Estadual do Centro-Oeste
Profª Drª Sheila Marta Carregosa Rocha – Universidade do Estado da Bahia

Medicina: ciências da saúde e pesquisa interdisciplinar 3

Diagramação: Camila Alves de Cremo
Correção: Flávia Roberta Barão
Indexação: Gabriel Motomu Teshima
Revisão: Os autores
Organizador: Benedito Rodrigues da Silva Neto

Dados Internacionais de Catalogação na Publicação (CIP)

M489 Medicina: ciências da saúde e pesquisa interdisciplinar 3 /
Organizador Benedito Rodrigues da Silva Neto. – Ponta
Grossa - PR: Atena, 2021.

Formato: PDF

Requisitos de sistema: Adobe Acrobat Reader

Modo de acesso: World Wide Web

Inclui bibliografia

ISBN 978-65-5983-468-6

DOI: <https://doi.org/10.22533/at.ed.686210809>

1. Medicina. 2. Saúde. I. Silva Neto, Benedito
Rodrigues da (Organizador). II. Título.

CDD 610

Elaborado por Bibliotecária Janaina Ramos – CRB-8/9166

Atena Editora

Ponta Grossa – Paraná – Brasil
Telefone: +55 (42) 3323-5493

www.atenaeditora.com.br

contato@atenaeditora.com.br

DECLARAÇÃO DOS AUTORES

Os autores desta obra: 1. Atestam não possuir qualquer interesse comercial que constitua um conflito de interesses em relação ao artigo científico publicado; 2. Declaram que participaram ativamente da construção dos respectivos manuscritos, preferencialmente na: a) Concepção do estudo, e/ou aquisição de dados, e/ou análise e interpretação de dados; b) Elaboração do artigo ou revisão com vistas a tornar o material intelectualmente relevante; c) Aprovação final do manuscrito para submissão.; 3. Certificam que os artigos científicos publicados estão completamente isentos de dados e/ou resultados fraudulentos; 4. Confirmam a citação e a referência correta de todos os dados e de interpretações de dados de outras pesquisas; 5. Reconhecem terem informado todas as fontes de financiamento recebidas para a consecução da pesquisa; 6. Autorizam a edição da obra, que incluem os registros de ficha catalográfica, ISBN, DOI e demais indexadores, projeto visual e criação de capa, diagramação de miolo, assim como lançamento e divulgação da mesma conforme critérios da Atena Editora.

DECLARAÇÃO DA EDITORA

A Atena Editora declara, para os devidos fins de direito, que: 1. A presente publicação constitui apenas transferência temporária dos direitos autorais, direito sobre a publicação, inclusive não constitui responsabilidade solidária na criação dos manuscritos publicados, nos termos previstos na Lei sobre direitos autorais (Lei 9610/98), no art. 184 do Código penal e no art. 927 do Código Civil; 2. Autoriza e incentiva os autores a assinarem contratos com repositórios institucionais, com fins exclusivos de divulgação da obra, desde que com o devido reconhecimento de autoria e edição e sem qualquer finalidade comercial; 3. Todos os e-book são *open access*, desta forma não os comercializa em seu site, sites parceiros, plataformas de *e-commerce*, ou qualquer outro meio virtual ou físico, portanto, está isenta de repasses de direitos autorais aos autores; 4. Todos os membros do conselho editorial são doutores e vinculados a instituições de ensino superior públicas, conforme recomendação da CAPES para obtenção do Qualis livro; 5. Não cede, comercializa ou autoriza a utilização dos nomes e e-mails dos autores, bem como nenhum outro dado dos mesmos, para qualquer finalidade que não o escopo da divulgação desta obra.

APRESENTAÇÃO

A interdisciplinaridade é fruto da tradição grega, onde os programas de ensino recebiam nome de *enkúklios Paidéia* e com objetivo de trabalhar a formação da personalidade integral do indivíduo, acumulando e justapondo conhecimentos e articulação entre as disciplinas. A partir da década de 70 esse conceito se tornou muito enfático em todos os campos do conhecimento, inclusive nas ciências médicas.

Sabemos que a saúde apresenta-se como campo totalmente interdisciplinar e também com alta complexidade, já que requer conhecimentos e práticas de diferentes áreas tais como as ambientais, clínicas, epidemiológicas, comportamentais, sociais, culturais etc. Deste modo, o trabalho em equipe de saúde, de forma interdisciplinar, compreende ações planejadas em função das necessidades do grupo populacional a ser atendido não se limitando às definições exclusivistas de cada profissional.

Tendo em vista a importância deste conceito, a Atena Editora nas suas atribuições de agente propagador de informação científica apresenta a nova obra no campo das Ciências Médicas intitulada “Medicina: Ciências da Saúde e Pesquisa Interdisciplinar” em seis volumes, fomentando a forma interdisciplinar de se pensar na medicina e mais especificadamente nas ciências da saúde. É um fundamento extremamente relevante direcionarmos ao nosso leitor uma produção científica com conhecimento de causa do seu título proposto, portanto, esta obra compreende uma comunicação de dados desenvolvidos em seus campos e categorizados em volumes de forma que ampliem a visão interdisciplinar do leitor.

Finalmente reforçamos que a divulgação científica é fundamental para romper com as limitações ainda existentes em nosso país, assim, mais uma vez parabenizamos a estrutura da Atena Editora por oferecer uma plataforma consolidada e confiável para estes pesquisadores divulguem seus resultados.

Desejo a todos uma proveitosa leitura!

Benedito Rodrigues da Silva Neto

SUMÁRIO

CAPÍTULO 1..... 1

A EVOLUÇÃO DO CONHECIMENTO ACERCA DAS MUTAÇÕES *TP53* E SEU IMPACTO PARA A OCORRÊNCIA DE TUMORES HEREDITÁRIOS

Larissa Dill Gazzola

Fabiana Sanson Zagonel

Juliana Ferreira da Silva

Karin Rosa Persegona Ogradowski

 <https://doi.org/10.22533/at.ed.6862108091>

CAPÍTULO 2..... 8

A INFLUÊNCIA DA TERAPIA NUTRICIONAL NO TRATAMENTO DO CÂNCER

João Paulo Pereira

Helder Cardoso Tavares

Cristiane Diogenes Bandeira Bulhões

Maria Algeni Tavares Landim

Rafaela Leandro de Lima

Edna Mori

 <https://doi.org/10.22533/at.ed.6862108092>

CAPÍTULO 3..... 17

A RELAÇÃO ENTRE A TERAPIA DE REPOSIÇÃO HORMONAL E O CÂNCER DE MAMA: REVISÃO DE LITERATURA

Maria Josilene Castro de Freitas

Fernanda Araújo Trindade

Rodolfo Marcony Nobre Lira

Ricardo Braga de Amorim

André Carvalho Matias

Raylana Tamires Carvalho Contente

Suellen Ferreira de Moura

Gisely Nascimento da Costa Maia

Roberta Nathalie Oliveira Silva

Taynah Cristina Marques Mourão

Marcielle Ferreira da Cunha Lopes

Dandara de Fátima Ribeiro Bendelaque

 <https://doi.org/10.22533/at.ed.6862108093>

CAPÍTULO 4..... 20

AGENTES ANTI-PD-1/PD-L1 NO CÂNCER DE MAMA TRIPLO NEGATIVO

Davi Fonseca Ferreira Silva

Márcia Cristina Pena Figueiredo

Geone Pimentel dos Santos Bulhões de Almeida

Bruno Coêlho Cavalcanti

Aníbal de Freitas Santos Júnior

Hemerson Iury Ferreira Magalhães

José Roberto de Oliveira Ferreira

 <https://doi.org/10.22533/at.ed.6862108094>

CAPÍTULO 5..... 34

ANÁLISE EPIDEMIOLÓGICA DO CÂNCER DE BOCA E OROFARINGE EM PACIENTES IDOSOS NO BRASIL NOS ÚLTIMOS 5 ANOS

Danilo Brito Nogueira
Leticia Ferreira Santos Brito
Maria Beatriz Meneses Melo
Elomar Rezende Moura
Yane Passos de Oliveira
Ryan Fernando Menezes
Ana Clara Gonçalves Ferreira Batista
Felipe Rafael Batista Rocha

 <https://doi.org/10.22533/at.ed.6862108095>

CAPÍTULO 6..... 36

APLICAÇÃO DA AURICULOTERAPIA COMO ADJUVANTE NO TRATAMENTO DE DOR ONCOLÓGICA EM PACIENTES SUBMETIDOS À ONCOTERAPIA

Murilo Elder Ferreira Costa
Ramon Ferreira Ribeiro
Armando Sequeira Penela
Thais Gomes Mateus
Remo Rodrigues Carneiro
João Paulo Saldanha Rodrigues
Érika Poça Cardoso
Ana Caroline Menezes Nunes
Hiago Vinícius Costa Silva
Valcilene Pereira da Costa Rodrigues
Kethelen Alana Matos Costa

 <https://doi.org/10.22533/at.ed.6862108096>

CAPÍTULO 7..... 46

CÂNCER DE COLO UTERINO NEUROENDOCRINO – RELATO DE CASO

Samuel Layanno de Sousa Carvalho
Lucas Santana Passos
Graciete Helena Nascimento dos Santos

 <https://doi.org/10.22533/at.ed.6862108097>

CAPÍTULO 8..... 52

CHARACTERIZATION OF NEURAL PRECURSORS OBTAINED FROM HUMAN ADIPOSE-DERIVED MESENCHYMAL STEM CELLS

Nathalia Barth de Oliveira
Ana Carolina Irioda
Priscila Elias Ferreira Stricker
Bassam Felipe Mogharbel
Nádia Nascimento da Rosa
Katherine Athayde Teixeira de Carvalho

 <https://doi.org/10.22533/at.ed.6862108098>

CAPÍTULO 9..... 65

DIAGNÓSTICO PRECOCE NO CÂNCER INFANTIL COMO ESTRATÉGIA PARA GARANTIR QUALIDADE DE VIDA

Beatriz Palácio Andrade
Caroline Wolff
Fernanda Lima Saldanha
Gabriel Moraes Saldanha Flor de Oliveira
Isabella Bezerra de Araújo Lacerda Lima
Letícia Amorim de Souza Nelson
Luciano Victor Vasconcelos Saldanha
Pedro Barbosa Ribeiro
Priscila Sabino dos Santos

 <https://doi.org/10.22533/at.ed.6862108099>

CAPÍTULO 10..... 73

DOR TOTAL DE MULHERES COM CÂNCER DE MAMA: UM RELATO DE EXPERIÊNCIA

Maria Clara Aguiar de Oliveira

 <https://doi.org/10.22533/at.ed.68621080910>

CAPÍTULO 11 81

EFEITOS DA TERAPIA A LASER DE BAIXA POTÊNCIA NO TRATAMENTO DE MUCOSITE ORAL EM PACIENTES SUBMETIDOS À ONCOTERAPIA DE CABEÇA E PESCOÇO

Ramon Ferreira Ribeiro
Murilo Elder Ferreira Costa
Armando Sequeira Penela

 <https://doi.org/10.22533/at.ed.68621080911>

CAPÍTULO 12..... 90

EFEITOS TERATOGENICOS CAUSADOS POR ANTI-HISTAMÍNICOS

Nara Assis Salgarello
Isadora Estefânio Coelho
Victor Rocha Moreira Antunes

 <https://doi.org/10.22533/at.ed.68621080912>

CAPÍTULO 13..... 94

LEVANTAMENTO DOS EFEITOS DE ORGANOFOSFORADOS SOBRE DIFERENTES SISTEMA ORGÂNICOS

Djanira Aparecida da Luz Veronez
Pietra Mancini Seibt
William Mattana dos Santos
Larissa Dayelle Osternack

 <https://doi.org/10.22533/at.ed.68621080913>

CAPÍTULO 14..... 111

MANIFESTO DE GLIOMAS E TUMORES MALIGNOS NO SISTEMA NERVOSO

Sérgio Manuel Coelho Fernando

Lucas dos Santos de Oliveira

 <https://doi.org/10.22533/at.ed.68621080914>

CAPÍTULO 15..... 113

MELANOMA COM METÁSTASE CARDÍACA: UMA REVISÃO DE LITERATURA

Bárbara Victoria Sena de Brito

João Rafael Pereira Bezerra Cavalcanti

Louenn Santos de Rezende

Luana Maria Leite Villarim Dias

 <https://doi.org/10.22533/at.ed.68621080915>

CAPÍTULO 16..... 121

METÁSTASE EM LINFONODO CERVICAL COMO APRESENTAÇÃO INICIAL DE CARCINOMA DE CÉLULAS ESCAMOSAS DE TONSILA PALATINA: RELATO DE CASO E REVISÃO DA LITERATURA

Tiago Seiki Gushiken Petrucci

Nábia Maria Moreira Salomão Simão

Argemiro José Terra Petrucci

 <https://doi.org/10.22533/at.ed.68621080916>

CAPÍTULO 17..... 132

O BAÇO E A MEDICINA REGENERATIVA

Tatiane Santos de Oliveira

Marluce da Cunha Mantovani

Sérgio Paulo Bydlowski

 <https://doi.org/10.22533/at.ed.68621080917>

CAPÍTULO 18..... 152

OSTEOGENESIS IMPERFECTA: UM NOVO PANORAMA ENVOLVENDO GENÉTICA, BIOMARCADORES E DIAGNÓSTICO PRECOCE

Solange Cristina Costa Cotlinsky

Wilhan Wiznieski Munari

Pâmella Thayse de Quadros Kassies

 <https://doi.org/10.22533/at.ed.68621080918>

CAPÍTULO 19..... 156

PERFIL CLÍNICO DE CRIANÇAS E ADOLESCENTES COM CÂNCER ADMITIDOS PELO HOSPITAL NAPOLEÃO LAUREANO

Thais Andrade de Araújo

Stéphanie Araújo de Andrade

Camila Pereira Nogueira

Vanessa Messias Muniz Fachine

Ana Paula Moraes Ventura

 <https://doi.org/10.22533/at.ed.68621080919>

CAPÍTULO 20..... 165

PRINCIPAIS SINTOMAS GASTROINTESTINAIS PRESENTES EM PACIENTES COM CÂNCER DE MAMA EM TRATAMENTO QUIMIOTERÁPICO DE UMA CLÍNICA PARTICULAR DO DISTRITO FEDERAL

Joyce Alves Lemos
Gislaine Queiroz da Silva
Daniela de Araújo Medeiros Dias
Paulina Nunes da Silva

 <https://doi.org/10.22533/at.ed.68621080920>

CAPÍTULO 21..... 170

RELAÇÃO ENTRE TABAGISMO E CÂNCER DO COLO DO ÚTERO

Beatriz Bertoletti Mota
Amanda Cechelero Cruz
Luíza Maria Rocca de Paula
Samya Hamad Mehanna

 <https://doi.org/10.22533/at.ed.68621080921>

CAPÍTULO 22..... 175

TIPOS DE PAPILOMA VÍRUS HUMANO (HPV) E SUA RELAÇÃO COM O CÂNCER DE COLO UTERINO

Gabriel Matias Borges Silvério
Gabriela Martins Rosini
Giovanni Di Lascio Sperotto
Júlia Cândido Dalmolin
Maria Cecília da Lozzo Garbelini
Nicole Ton
Oscar de Almeida Júnior

 <https://doi.org/10.22533/at.ed.68621080922>

CAPÍTULO 23..... 184

USO PROLONGADO DE INIBIDORES DA BOMBA DE PRÓTONS E NEOPLASIA GASTROINTESTINAL: UMA REVISÃO DE LITERATURA

Crístia Rosineiri Gonçalves Lopes Corrêa
Diúle Nunes Sales
Maria Clara Lopes Rezende
Mariana Schmidt Cheaitou
Sofia d'Anjos Rodrigues
Vitor de Paula Boechat Soares

 <https://doi.org/10.22533/at.ed.68621080923>

SOBRE O ORGANIZADOR..... 193

ÍNDICE REMISSIVO..... 194

CAPÍTULO 8

CHARACTERIZATION OF NEURAL PRECURSORS OBTAINED FROM HUMAN ADIPOSE-DERIVED MESENCHYMAL STEM CELLS

Data de aceite: 01/09/2021

Data de submissão: 04/06/2021

Nathalia Barth de Oliveira

Advanced Therapy and Cellular Biotechnology
in Regenerative Medicine Department,
Pelé Pequeno Príncipe Institute, Child and
Adolescent Health Research and Pequeno
Príncipe Faculties
Curitiba – Paraná – Brazil
<http://lattes.cnpq.br/8866080887373071>

Ana Carolina Irioda

Advanced Therapy and Cellular Biotechnology
in Regenerative Medicine Department,
Pelé Pequeno Príncipe Institute, Child and
Adolescent Health Research and Pequeno
Príncipe Faculties
Curitiba – Paraná – Brazil
<http://lattes.cnpq.br/2869392384748012>

Priscila Elias Ferreira Stricker

Advanced Therapy and Cellular Biotechnology
in Regenerative Medicine Department,
Pelé Pequeno Príncipe Institute, Child and
Adolescent Health Research and Pequeno
Príncipe Faculties
Curitiba – Paraná – Brazil
<http://lattes.cnpq.br/7617706302599916>

Bassam Felipe Mogharbel

Advanced Therapy and Cellular Biotechnology
in Regenerative Medicine Department,
Pelé Pequeno Príncipe Institute, Child and
Adolescent Health Research and Pequeno
Príncipe Faculties
Curitiba – Paraná – Brazil
<http://lattes.cnpq.br/5953351155176699>

Nádia Nascimento da Rosa

Advanced Therapy and Cellular Biotechnology
in Regenerative Medicine Department,
Pelé Pequeno Príncipe Institute, Child and
Adolescent Health Research and Pequeno
Príncipe Faculties
Curitiba – Paraná – Brazil
<http://lattes.cnpq.br/5518492186320543>

Katherine Athayde Teixeira de Carvalho

Advanced Therapy and Cellular Biotechnology
in Regenerative Medicine Department,
Pelé Pequeno Príncipe Institute, Child and
Adolescent Health Research and Pequeno
Príncipe Faculties
Curitiba – Paraná – Brazil
<http://lattes.cnpq.br/6520738424498523>

ABSTRACT: Mesenchymal stem cells have been the focus of several studies, as they can be isolated from any vascularized tissue and can differentiate into mesodermal and non-mesodermal lineages. Adipose tissue is considered a good source for these cells, as it has a high yield in isolation and a greater capacity to form colonies. Regarding their differentiation capacity, mesenchymal stem cells from adipose tissue can differentiate into several *in vitro* lineages, such as adipogenic, chondrogenic, osteogenic, and neurogenic. During neurogenic differentiation, neurospheres, composed of neural precursors, are formed. These cells can be a potential alternative in treating neurodegenerative diseases such as Alzheimer's and Parkinson's. However, for the safe and effective use of these cells in regenerative medicine, immunophenotypic and

genotypic characterization is necessary and xenofree conditions. Therefore, this study aimed to characterize neural precursors derived from adipose tissue mesenchymal stem cells. For that, cells from the adipose tissue were isolated and cultured, expanded, and submitted to trilineage differentiation. The characterization of undifferentiated cells was carried out through flow cytometry which indicated that the isolated cells had characteristics of mesenchymal stem cells. The differentiation in neural precursors occurred through the formation of neurospheres after seeding the cells over a natural functional biopolymer matrix, called NFBX. Cells subjected to differentiation were positive for expression of Nestin and β tubulin-III proteins in immunocytochemistry. Also, they expressed NEFM and TUBB3 genes in RT-PCR, indicating the characteristic neural phenotype of these differentiated cells and the epigenetic determination of this matrix in the differentiation of mesenchymal stem cells to neurospheres.

KEYWORDS: mesenchymal stem cells, adipose tissue, neurospheres, neural precursor, biopolymer.

CARACTERIZAÇÃO DE PRECURSORAS NEURONAIS DERIVADAS DE CÉLULAS-TRONCO MESENQUIMAIS DO TECIDO ADIPOSE

RESUMO: As células-tronco mesenquimais têm sido o foco de diversos estudos na atualidade, pois podem ser isoladas a partir de qualquer tecido vascularizado e são capazes de se diferenciar em linhagens mesodermais e não mesodermais. O tecido adiposo é considerado uma boa fonte para obtenção dessas células, pois apresenta um alto rendimento no isolamento e uma maior capacidade de formar colônias. Com relação à sua capacidade de diferenciação, as células-tronco mesenquimais do tecido adiposo podem se diferenciar em diversas linhagens *in vitro* como, adipogênica, condrogênica, osteogênica e neurogênica. Durante a diferenciação neurogênica ocorre a formação de neuroesferas, que são compostas por precursoras neuronais, as quais são uma potencial alternativa no tratamento de doenças neurodegenerativas como o Alzheimer e o Parkinson. Contudo, para a utilização segura e eficaz dessas células na medicina regenerativa é necessária uma caracterização imunofenotípica e genotípica, assim como ser um processo livres de produtos de origem animal. Sendo assim, o objetivo desse estudo foi caracterizar as precursoras neuronais derivadas das células-tronco mesenquimais do tecido adiposo. Para isso, foram isoladas células do tecido adiposo que foram cultivadas, expandidas e, em seguida, submetidas à diferenciação *trilineage*. A caracterização das células indiferenciadas foi realizada por meio da citometria de fluxo que indicou que as células isoladas apresentaram características de células-tronco mesenquimais. A diferenciação em precursoras neuronais se deu por meio da formação de neuroesferas após a semeadura das células sobre uma matriz funcional de biopolímero natural, denominada NFBX. As células submetidas à diferenciação foram positivas para expressão das proteínas Nestina e β tubulina-III na imunocitoquímica. Além disso, expressaram os genes NEFM e TUBB3 em RT-PCR, indicando o fenótipo neuronal característico dessas células diferenciadas e a determinação epigenética dessa matriz na diferenciação de células-tronco mesenquimais em neuroesferas.

PALAVRAS-CHAVE: células-tronco mesenquimais, tecido adiposo, neuroesferas, precursoras neuronais, biopolímero.

1 | INTRODUCTION

Currently, mesenchymal stem cells (MSCs) are in focus, as they can be isolated from any vascularized tissue and have high plasticity with the ability to originate mesodermal and non-mesodermal tissues. In addition, they secrete pro and anti-inflammatory cytokines and growth factors that provide modulation of the inflammatory response and tissue repair, contributing to the body's homeostasis (BACAKOVA et al., 2018; BATEMAN et al., 2018; BROWN et al., 2019; HAN et al., 2019).

Adipose tissue is derived from the embryonic mesoderm and has a diverse population of cells, including MSCs, capable of differentiating into osteoblasts, chondroblasts, cardiac myocytes, smooth muscle cells, and neural cells. Therefore, mesenchymal stem cells from adipose tissue (ASCs) are considered great candidates for regenerative medicine due to their wide differentiation capacity and their role in homeostasis and tissue repair throughout the life of adult organisms (MAZZEO; SANTOS, 2018; MIANA; GONZÁLEZ, 2018; SI et al., 2019).

The neurodifferentiation capacity of ASCs has made them promising for studies aimed at the treatment of neurodegenerative diseases. During neurogenic differentiation, cells form small spheres, called neurospheres, composed of neural precursors (NP), a mixed population of stem cells, and neural progenitors (LEE; LOUIS; REYNOLDS, 2015; MENDES FILHO et al., 2018; ZHANG et al., 2012). However, using these NPs in clinical treatments, it is necessary to expand the knowledge about the proteins and genes that these cells express. Consequently, basic studies such as the characterization of NPs derived from ASCs are needed, as they may assist future clinical projects enabling the safe and effective use of these cells.

2 | METHOD

The project used samples of adipose tissue, taken from healthy patients, over 18 years old, who signed the free and informed consent form, after approved by the ethics committee of Pequeno Príncipe Faculties (CEP / FPP) under the number: 3,049,033 on 11/30/2018.

2.1 Isolation, cultivation and expansion of ASCs

The samples were washed extensively with phosphate-buffered saline (PBS) containing 1% penicillin and streptomycin (P / S), were enzymatically digested with 0.075% type I collagenase at 37°C under continuous agitation for 30 minutes. After incubation, collagenase type I activity was inactivated by adding an equal volume of Dulbecco/F12 modified Eagle (DMEM/F12), containing 10% fetal bovine serum (SFB) and 1% P/S (standard culture medium). Subsequently, the samples were centrifuged at 600g for 10 minutes, and filtered through a 100 μ M mesh. Cells were plated (10^5 cells/cm²) in 75 cm²

culture flasks with standard culture medium and incubated at 37°C and 5% CO² (adapted from BUNNELL et al., 2008; IRIODA et al., 2016; ZUK et al., 2002).

When the adherent cells reached confluence, they were detached by trypsin / EDTA (0.25%) (Sigma, St. Louis, MO - USA) for 5 minutes. The released cells were collected and replated for subculturing in culture flasks with the same culture medium. This process repeated until the cells reached passage 4 (P4) for analysis.

2.2 Trilineage differentiation

The cells were seeded in 24-well culture plates (10⁴ cells per well). After reaching 80% confluence, the plates were treated with a specific differentiation medium. Cells were fixed with 4% paraformaldehyde (Sigma-Aldrich®, USA) for 20 minutes and then performed the stains.

Adipogenic differentiation was induced in standard culture medium supplemented with 0.5 µM dexamethasone (Sigma-Aldrich®, USA), 0.5 mM isobutyl-methylxanthine (Sigma-Aldrich®, USA), and 50 µM indomethacin (Sigma-Aldrich®, USA). Cultivation with differentiation medium was maintained for 14 days and the medium was changed twice a week. The accumulation of lipid vesicles was detected by staining Oil Red O cells (Sigma-Aldrich®, USA) (BUNNELL et al., 2008; IRIODA et al., 2016).

Osteogenic differentiation was induced with standard culture medium supplemented with 1 nM dexamethasone (Sigma-Aldrich®, USA), 2 mM β-glycerol-phosphate (Sigma-Aldrich®, USA), and 50 µM ascorbate-2-phosphate (Sigma-Aldrich®, USA). The cells were cultured in this medium for 35 days. Mineralization was evaluated by staining the cells with 40 mM Alizarin Red (adapted from BUNNELL et al., 2008; IRIODA et al., 2016).

For chondrogenic differentiation, the cells were resuspended at a concentration of 1.6X10⁷ cells / mL, then 5 µL of the cell suspension was transferred to the center of the well of a 24-well plate and kept for two hours at 37 ° C. After incubation, the differentiation medium was added according to the manufacturer's specifications (StemPro® Chondrogenesis Differentiation Kit - GIBCO™ Life Technologies, USA). This medium was changed twice a week for a period of 14 days, and the production of proteoglycans was stained with the Alcian Blue in acidic pH (IRIODA et al., 2016; ZUK et al., 2001).

2.3 Differentiation in neural precursors

For the differentiation of ASCs into NPs, the NFBX membrane was placed in 24-well plates, sterilized under UV light, and hydrated with a standard culture medium. After 24 hours the medium was removed from the wells and the cells were seeded on the membrane at a concentration of 1X10⁴ in 20 µl of standard medium and incubated at 37°C and 5% CO² for 20 minutes. After this period, 500 µl of the standard medium was added to each well. The medium was changed twice a week until the neurospheres were obtained. With the aid of a 1000 µL micropipette, the neurospheres were removed from the wells and transferred to 75

cm² bottles for expansion and 6- and 48-well plates for analysis.

2.4 Flow cytometry

Undifferentiated cells were analyzed for the expression of surface markers, using monoclonal antibodies against specific antigens conjugated to fluorochromes (CD13, CD34, CD45, CD73, CD90, CD105, HLA-DR, and HLA-ABC) and analyzed by flow cytometry.

After trypsinization, cells were resuspended in 1mL PBS with 5% human albumin (5% PBS / HA). Then, 200 μ L of the suspension were distributed in cytometry tubes, the conjugated antibodies were added, the tubes were vortexed and incubated in the dark for 15 minutes. After incubation, 400 μ L of 5% PBS / HA was added and the tubes were vortexed again, the supernatant was discarded and the cells were resuspended with 100 μ L of 5% PBS / HA. 5 μ L of 7-AAD (7-aminoactinomycin D) was added to the specific tubes and the cells were incubated for 5 minutes. After incubation, 400 μ L of 5% PBS / HA were added to each tube, followed by analysis on the flow cytometer (FACS Canto II; Becton Dickinson, USA) (CARVALHO et al., 2008; IRIODA et al., 2016), 10,000 cells were analyzed and data analysis was performed using the Infinicyt™ software: Flow Cytometry Software 1.6.0 (Cytognos S.L., Spain).

2.5 Immunocytochemistry

Undifferentiated cells and neurospheres were characterized by the expression of Nestin and β III-tubulin proteins. After the neurosphere dissociation, cells were washed with PBS and fixed with 4% paraformaldehyde for 20 minutes. The cells were permeabilized with 0.1% Triton X-100 (Amresco®, USA) diluted in PBS with 1% human albumin (1% PBS/HA) for 30 minutes. After incubation, the wells were washed with PBS and the primary antibodies diluted in 1% PBS / HA were added, which were incubated overnight at 4 °C. After incubation, the solutions with the primary antibodies were discarded and the wells washed with PBS. The cells were incubated for 1 hour at room temperature with the secondary antibody diluted in 1% PBS / HA, in the absence of light. After incubation, the wells were washed and 300 μ L of PBS was added with 1 μ g / mL of Hoechst 33258 (Invitrogen®M - USA) to identify the nucleus (adapted from TRZASKA; RAMESHWAR, 2011). Immunocytochemical analyzes were performed using an inverted fluorescence microscope (Axio Vert. A1 – Zeiss, Oberkochen- Germany).

2.6 RT-PCR

The neurospheres were grown in 6-well plates with a standard culture medium changed twice a week. When the cells reached confluence, they were submitted to the RNA extraction protocol that was carried out following the instructions of the manufacturer of the kit “PureLink™ RNA Mini Kit” (Invitrogen®M - USA). cDNA production was performed following the instructions of the “High-Capacity cDNA Reverse Transcription Kit” kit (Invitrogen®M

– USA). The primer' sequences (forward and reverse), molecular weight of the amplified material, and annealing temperature are described in TABLE 1.

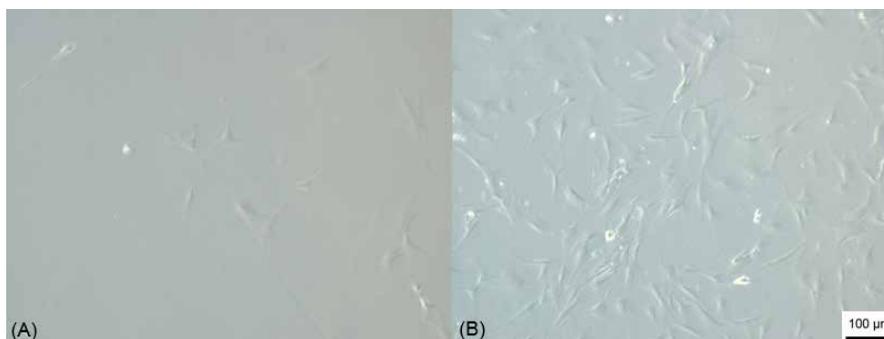
GENE	PRIMERS	*AT (°C)	AMPLIFIED SIZE (bp)**
<i>NEFM</i>	F: 5'ACATCGAGAGCGCCACAA3' R: 5'GACGAGCCATTCCCACCTTTG3'	60	98
<i>ACTB</i>	F: 5'CTGGGACGACATGGAGAAA3' R:5'AAGGAAGGCTGGAAGAGTGC3'	57	564
<i>TUBB3</i>	F: 5'GGAGATCGTGCACATCCAGG3' R: 5' CAGGCAGTCGCAGTTTTTCAC'	62	385

Note: Primers obtained from Sigma Aldrich®. * AT (°C) = annealing temperature of the primer in degrees Celsius. ** (bp) = base pairs. Source: Author (2019).

TABLE 1 - PRIMERS USED IN THE RT-PCR REACTION.

3 | RESULTS AND DISCUSSION

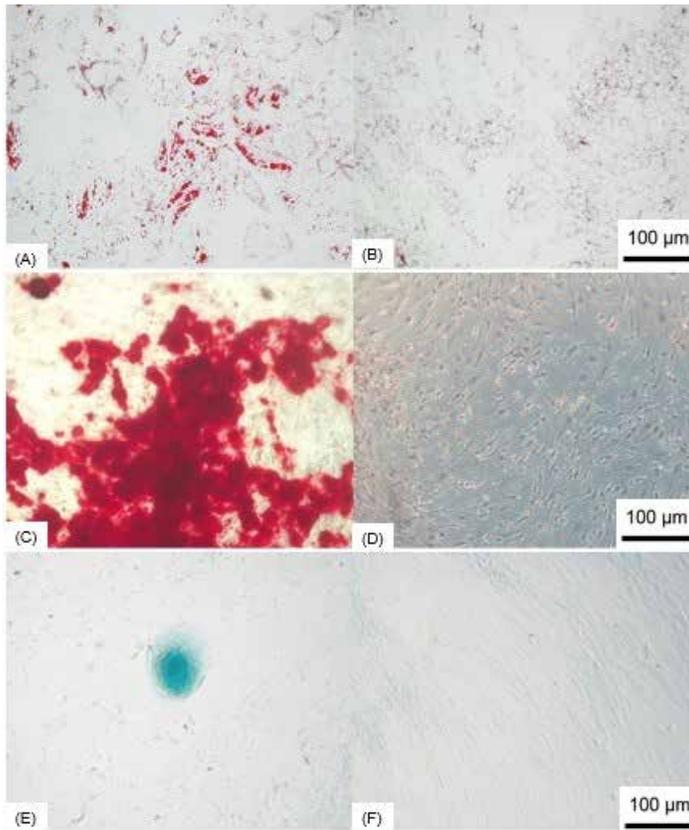
The 20 isolated samples were identified from A1 to A20 according to the order of collection. During the isolation process, the contaminating blood cells were removed after successive washes with PBS, the isolated cells adhered to the plastic and showed fibroblast morphology in approximately 3 days of culture, the cell confluence was reached after an average time of 10 days (FIGURE 1) (BORKOWSKA et al., 2015). In the study by Zuk et al. (2001), the confluence was reached in about 48 hours, but the cell concentration used in the plating is not reported, thus the difference in the confluence time may be related to the plating concentration, which in the present study was 10^5 cells/cm² for each 75cm² bottle. Cells were grown until P4 for analysis.



(A) Cells 3 days after isolation showing fibroblast morphology. (B) Cells with 80% confluence. (Source: The Author, 2019. Image obtained by inversion optical microscopy, 100X - Axio Vert. A1 - Zeiss, Germany). Scale bar, 100 µm.

FIGURE 1 – ASCs CULTIVATION.

Eight samples were chosen at random to be submitted to *trilineage* differentiation. All samples were able to differentiate in the three strains, the adipocytes showed lipid vacuoles stained with Oil Red O (FIGURE 2a), in the osteoblasts it was possible to observe the mineralization through the staining with red alizarin (FIGURE 2c) and, the differentiation in chondroblasts was proven by staining proteoglycans with blue Alcian (FIGURE 2e).



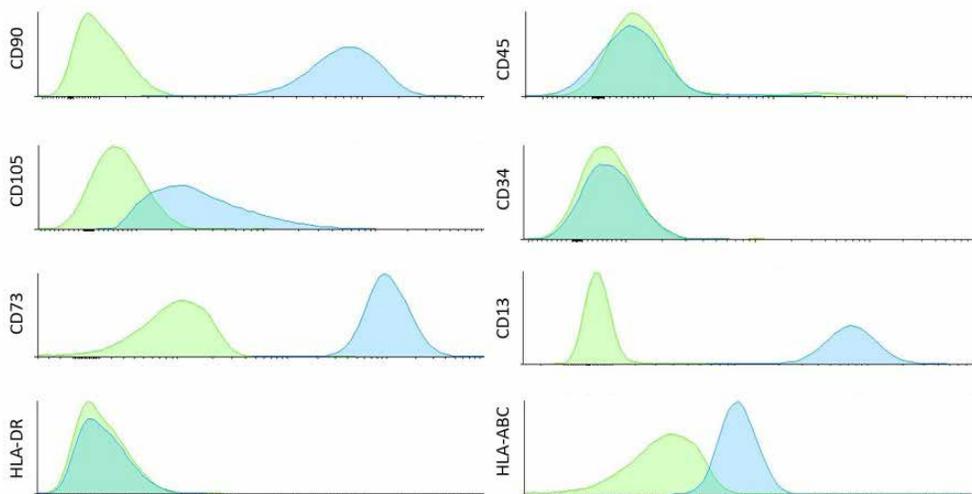
(A) ASCs subjected to adipogenic differentiation, staining the lipid vacuoles with Oil Red O. (B) Control of undifferentiated ASCs. (C) ASCs submitted to osteogenic differentiation showing mineralization stained by red alizarin. (D) Undifferentiated control. (E) ASCs differentiated in chondroblasts with the production of proteoglycans stained with Alcian blue. (F) Undifferentiated control. (Source: O Autor, 2019. Image obtained by inversion optical microscopy, 100X - Axio Vert. A1 - Zeiss, Germany). Scale bar, 100 μm .

FIGURE 2 - *TRILINEAGE* DIFFERENTIATION.

Flow cytometry was performed on 12 samples and the histograms of the sample A15 are shown in FIGURE 3. The results show that more than 80% of the cells showed positive expression of CD13, CD73, CD90, CD105, and HLA-ABC and were negative for CD45 and HLA-DR. All samples showed an expression of less than 20% of CD34 which may show positivity at the beginning of culture, however, after successive passages, this positivity

tends to disappear (BOURIN et al., 2013).

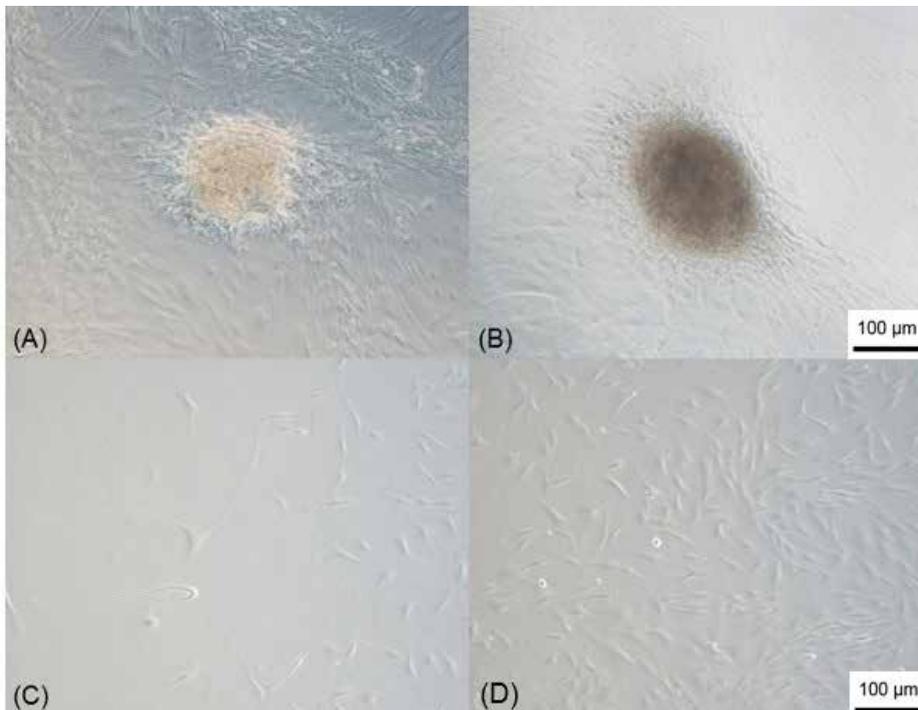
According to the International Society for Cell Therapy and the International Federation for Therapeutics and Adipose Science, ASCs must be adherent to plastic, capable of differentiating into adipocytes, osteoblasts, and chondroblasts, they must present a positive expression above 80% for CD13, CD73, CD90, and CD105, must be negative for CD45 (<2%) and, CD34 is considered an unstable marker that can be positive in up to 20% of cells (BOURIN et al., 2013).



Histograms for the analysis of flow cytometry of the sample A15. The blue peak represents positivity for CD90, CD105, CD73, CD13, and HLA-ABC and negativity for CD34, CD45, and HLA-DR markers; and in green, the isotypic control demarcating the area in which the samples are negative for a specific marker. Source: Author (2020).

FIGURE 3 – HISTOGRAMS.

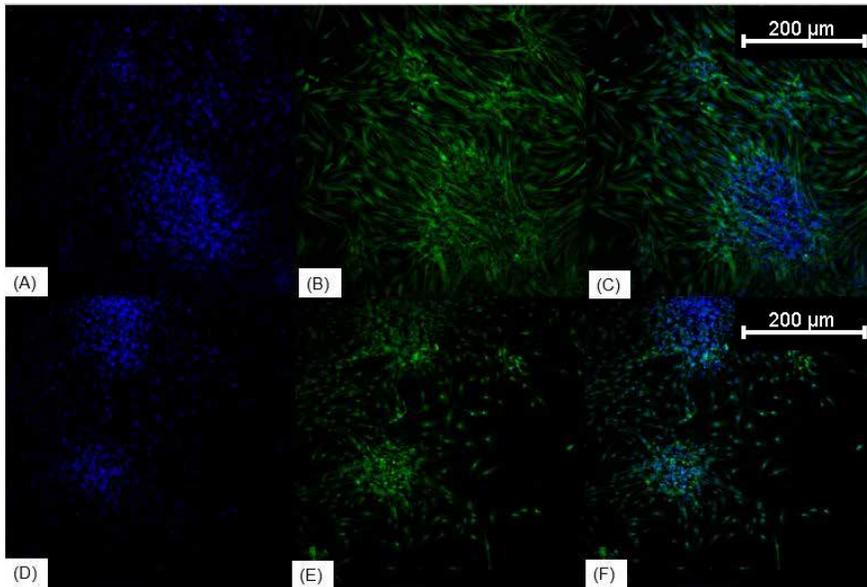
The production of neurospheres is crucial for the efficiency of neural differentiation, and most protocols use high-cost supplements or gene transfection (BORKOWSKA et al., 2015). In this study, the differentiation in NPs was through the formation of neurospheres that took place after 15-20 days of cultivation on the NFBX membrane (FIGURE 4). In the study by Zhang et al. (2012) neurospheres formation could be observed after approximately 7-9 days, but they used a neurobasal medium supplemented with epidermal growth factor (EGF), basic fibroblast growth factor (bFGF), and B27. The present study did not use any neurogenic growth factor or neurobasal medium, only the standard culture medium and the plating on the NFBX membrane. Therefore, the difference in the formation time of neurospheres may be related to the supplementation of the differentiation medium.



(A) Neurosphere formation process. (B) Neurosphere formed. (C) Expansion of NPs. (D) Expansion with 80% confluence. (Source: O Autor, 2019. Image obtained by inversion optical microscopy, 100X - Axio Vert. A1 - Zeiss, Germany). Scale bar, 100 μ m.

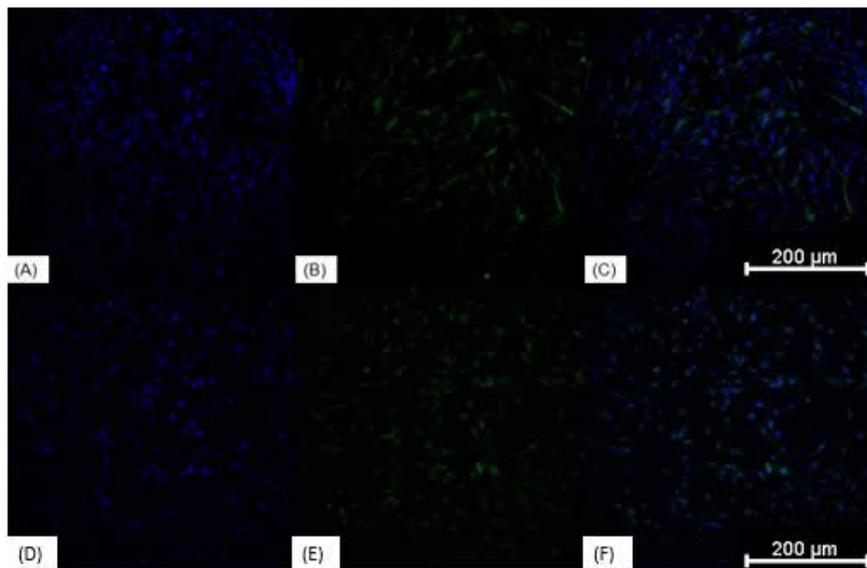
FIGURE 4 - NEUROSPHERE FORMATION AND EXPANSION.

At the end of neurogenic induction, samples A3, A9, A13, and A19 were submitted to the immunocytochemistry protocol and showed positive marking for β III-tubulin and Nestin (FIGURE 5) as well as the undifferentiated cells (FIGURE 6). ASCs can express early and late neural markers, about 1-5% of the cells are positive for Nestin, however, this expression decreases as the number of passages increases. β III-tubulin is positive in about 90% of cells regardless of passage (FOUDAH et al., 2014).



(A) Neurospheres showing hoescht marking on the nucleus (blue). (B) Neurospheres with anti- β III-tubulin antibody (FITC). (C) Images A and B overlapping. (D) Neurospheres showing hoescht marking on the nucleus (blue). (E) Neurospheres with anti-nestin antibody (FITC). (F) Images D and E overlapping (Source: O Autor, 2021. Image obtained by Fluorescence optical inversion microscope, 100X - Axio Vert. A1 - Zeiss, Germany). Scale bar, 200 μ m.

FIGURE 5 – IMMUNOCYTOCHEMISTRY OF NEUROSPHERES.

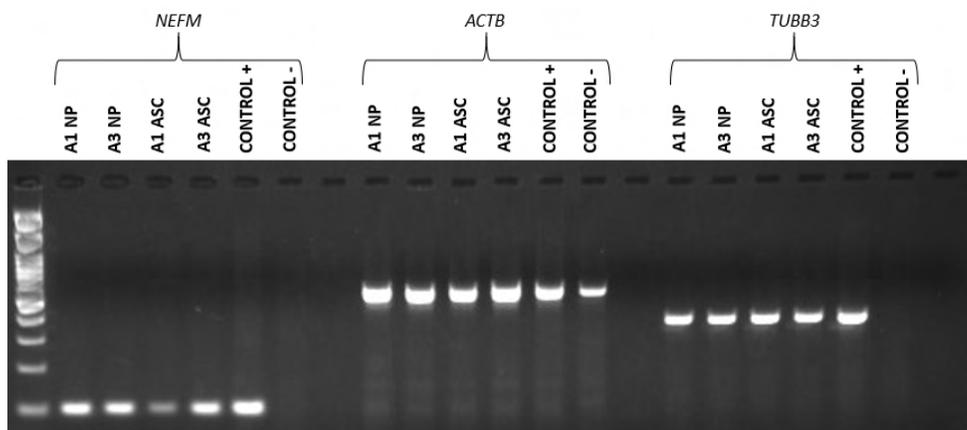


(A) ASCs showing Hoescht marking on the nucleus (blue). (B) ASC labeled with anti- β III-tubulin antibody (FITC). (C) Images A and B overlapping. (D) ASCs with Hoescht marking on the nucleus (blue). (E) ASC labeled with anti-nestin antibody (FITC). (F) Images D and E overlapping (Source: O Autor, 2021. Image obtained by Fluorescence optical inversion microscope, 100X - Axio Vert. A1 - Zeiss, Germany). Scale bar, 200 μ m.

FIGURE 6 - IMMUNOCYTOCHEMISTRY OF ASCs.

RT-PCR analysis was performed for *NEFM*, *TUBB3*, and *ACTB* genes. The *NEFM* gene encodes a medium neurofilament protein that is commonly used as a biomarker of neural damage, and its expression is mostly concentrated in the brain and cerebellum (STROUS et al., 2007). The *TUBB3* gene encodes a protein expressed mainly in neurons that is involved in neurogenesis, orientation, and maintenance of axons, its expression is mainly concentrated in the fetal brain (ÖZTOP et al., 2019). The *ACTB* gene is a constitutive gene and was used as a control and validation of the technique.

ASCs express neural marker genes at the transcription level and, after neurogenic induction, this expression increases (ZHENG et al., 2017). In the present study, both the undifferentiated cells and the neurosphere-derived NPs expressed the three genes analyzed (FIGURE 7), but the quantification was not performed. The “ReNcell™ CX Human Neural Progenitor Cell Line” cell line was used as a positive control (Millipore Cat. No. SCC007) and human fibroblasts were used as a negative control.



RT-PCR for amplification of *NEFM* (98bp), *ACTB* (564bp) and *TUBB3* (385bp) genes in ASCs and NPs (Source: O Autor, 2021).

FIGURE 7 – RT-PCR ANALYSIS OF ASCs and NPs.

4 | CONCLUSION

This study demonstrated that ASCs could differentiate into cells with neural characteristics phenotype through cultivation on the NFBX membrane, without adding neurogenic growth factors in the culture medium or gene transfection. Future studies will be necessary to quantify the expression of neural markers both in ASCs and in NPs derived from the neurospheres. Furthermore, the study provides evidence on the ability of ASCs to respond to environmental stimuli and define the fate of cell differentiation as an epigenetic factor, like this used matrix.

REFERENCES

- BACAKOVA, L. et al. Stem cells: their source, potency and use in regenerative therapies with focus on adipose-derived stem cells - a review. **Biotechnology Advances**, v. 36, n. 4, p. 1111–1126, Aug. 2018.
- BATEMAN, M. et al. Using Fat to Fight Disease: A Systematic Review of Non - Homologous Adipose - Derived Stromal / Stem Cell Therapies. **STEM CELLS**, v. 36, Feb 1 2018.
- BORKOWSKA, P. et al. Differentiation of adult rat mesenchymal stem cells to GABAergic, dopaminergic and cholinergic neurons. **Pharmacological reports: PR**, v. 67, n. 2, p. 179–186, abr. 2015.
- BOURIN, P. et al. Stromal cells from the adipose tissue-derived stromal vascular fraction and culture expanded adipose tissue-derived stromal / stem cells: a joint statement of the International Federation for Adipose Therapeutics and Science (IFATS) and the International Society for Cellular Therapy (ISCT). **Cytotherapy**, v. 15, n. 6, p. 641–648, Jun. 2013.
- BROWN, C. et al. Mesenchymal stem cells: Cell therapy and regeneration potential. **Journal of Tissue Engineering and Regenerative Medicine**, v. 13, n. 9, p. 1738–1755, set. 2019.
- BUNNELL, B. A. et al. Adipose-derived stem cells: isolation, expansion and differentiation. **Methods (San Diego, Calif.)**, Vol. 45, n. 2, p. 115–120, Jun. 2008.
- CARVALHO, K.A.T. et al. Angiogenesis without functional outcome after mononuclear stem cell transplant in a doxorubicin-induced dilated cardiomyopathy murine model. **The International Journal of Artificial Organs**, v. 31, n. 5, p. 431–438, May 2008.
- FOUDAH, D. et al. Expression of neural markers by undifferentiated mesenchymal-like stem cells from different sources. **Journal of Immunology Research**, vol. 2014, p. 987678, 2014.
- HAN, Y. et al. Mesenchymal Stem Cells for Regenerative Medicine. **Cells**, v. 8, n. Aug 8, 13. 2019.
- IRIODA, A. C. et al. Human Adipose-Derived Mesenchymal Stem Cells Cryopreservation and Thawing Decrease $\alpha 4$ -Integrin Expression. **Stem Cells International**, v. 2016, p. e2562718, 15 fev. 2016.
- LEE, V. M. ; LOUIS, SHARON A. ; REYNOLDS, BRENT A. The Central Nervous System. **Neural Stem Cells**, p. 6, abr. 2015.
- MAZZEO, A. ; SANTOS, E. J. C. Nanotechnology and multipotent adult progenitor cells in Reparative Medicine: therapeutic perspectives. **Einstein (São Paulo)**, v. Nov 16, 29 2018.
- MENDES FILHO, D. et al. Therapy With Mesenchymal Stem Cells in Parkinson Disease: History and Perspectives. **The Neurologist**, v. 23, n. 4, p. 141–147, jul. 2018.
- MIANA, V. V. ; GONZÁLEZ, E. A. P. Adipose tissue stem cells in regenerative medicine. **ecancermedicalsecience**, v. 12, 28 mar. 2018.
- ÖZTOP, S. et al. Class III β -tubulin Expression in Colorectal Neoplasms Is a Potential Predictive Biomarker for Paclitaxel Response. **Anticancer Research**, v. 39, n. 2, p. 655–662, Feb. 2019.

SI, Z. et al. Adipose-derived stem cells: Sources, potency, and implications for regenerative therapies. **Biomedicine & Pharmacotherapy = Biomedicine & Pharmacotherapie**, v. 114, p. 108765, Jun. 2019.

STROUS, R. D. et al. Association of the dopamine receptor interacting protein gene, NEF3, with early response to antipsychotic medication. **International Journal of Neuropsychopharmacology**, v. 10, n. 3, p. 321–333, 1 Jun. 2007.

TRZASKA, K. A. ; RAMESHWAR, P. Dopaminergic neural differentiation protocol for human mesenchymal stem cells. **Methods in Molecular Biology (Clifton, N.J.)**, v. 698, p. 295–303, 2011.

ZHANG, H.-T. et al. Neural differentiation ability of mesenchymal stromal cells from bone marrow and adipose tissue: a comparative study. **Cytotherapy**, v. 14, n. 10, p. 1203–1214, 1 set. 2012.

ZHENG, Y. et al. Comparison of the neural differentiation abilities of bone marrow - derived and adipose tissue - derived mesenchymal stem cells. **Molecular Medicine Reports**, v. 16, n. 4, p. 3877–3886, out. 2017.

ZUK, P.A. et al. Multilineage cells from human adipose tissue: implications for cell-based therapies. **Tissue Engineering**, v. 7, n. 2, p. 211–228, abr. 2001.

ZUK, P. A. et al. Human adipose tissue is a source of multipotent stem cells. **Molecular Biology of the Cell**, vol. 13, n. 12, p. 4279–4295, ten. 2002.

ÍNDICE REMISSIVO

A

Aconselhamento genético 1, 6
Auriculoterapia 36, 37, 38, 39, 40, 41, 42, 43, 44
Avaliação nutricional 8, 10, 11, 12, 15, 16, 169

B

Baço 49, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146
Biopolímero 53

C

Câncer 1, 3, 4, 5, 8, 9, 10, 11, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 25, 26, 27, 28, 29, 30, 32, 34, 36, 37, 38, 41, 43, 44, 46, 49, 50, 51, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 85, 86, 102, 113, 114, 115, 116, 117, 119, 122, 132, 145, 156, 157, 158, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 175, 176, 177, 178, 179, 180, 181, 182, 186, 188, 189, 190, 191
Câncer de mama 4, 10, 17, 18, 19, 20, 21, 22, 23, 26, 27, 28, 29, 30, 41, 73, 74, 75, 76, 77, 78, 79, 80, 165, 166, 167, 168, 169
Câncer de mama triplo negativo 20, 21, 23, 26, 27, 28, 29, 30
Câncer pediátrico 66, 156, 157, 160, 163, 164
Câncer uterino 175, 176, 177, 178, 180
Carcinoma 7, 28, 29, 31, 35, 46, 47, 48, 49, 50, 51, 120, 121, 122, 123, 124, 129, 130
Carcinoma em tonsila palatina 121
Células-tronco mesenquimais 53, 100, 141
Colo uterino 46, 49, 50, 51, 130, 170, 172, 173, 175, 176, 177, 178, 179, 180
Compostos organofosforados 94, 99, 100, 101, 103
Coração 101, 113, 114, 118, 132
Corpo humano 94, 114, 115

D

Descelularização 132, 133, 135, 144
Diagnóstico 1, 2, 3, 5, 8, 10, 11, 12, 13, 34, 48, 49, 50, 51, 65, 66, 67, 68, 69, 70, 71, 72, 74, 76, 77, 111, 113, 115, 116, 118, 119, 122, 129, 130, 133, 152, 153, 156, 158, 159, 161, 163, 164, 165, 166, 167, 175, 176, 178, 179, 182
Doença de Lobstein 153
Dor oncológica 36, 37, 38, 39, 40, 41, 42, 43, 44

E

Engenharia tecidual 132, 133, 135
Epidemiologia 35, 119, 175, 176, 180
Expectativa de vida 65
Expressão gênica 153

G

Genes supressores 1, 122, 123, 129
Gravidez 74, 90, 91, 92

H

Herbicidas 94
Hipergastrinemia 184, 185, 188
Hospital Napoleão Laureano 156, 157, 158, 159, 161, 162, 163, 164
HPV 46, 47, 48, 50, 69, 121, 122, 128, 129, 130, 131, 170, 171, 172, 173, 175, 176, 177, 178, 180, 181, 182, 183

I

Influência 8, 9, 11, 30, 121, 188
Inibidores 10, 13, 22, 23, 25, 26, 30, 184, 185, 186, 187, 188
Inseticidas 94
IST 175, 176

M

Medicina regenerativa 53, 132, 133, 134, 135, 138, 139, 140, 141, 142, 143, 144, 145, 146
Melanoma 21, 29, 66, 74, 113, 114, 115, 116, 117, 118, 119, 120
Menopausa 17, 18, 19, 74, 75
Metástase 113, 114, 115, 116, 117, 118, 121, 129, 175, 177, 178
Metástase linfonodal 121, 129

N

Neoplasia gastrointestinal 184, 185, 186, 188, 190
Neoplasias bucais 35
Neoplasias da mama 73
Neoplasias orofaríngeas 35
Neuroesferas 53

Neurologia 111

Nutrição 8, 15, 16, 82, 156, 169

O

Oncologia 6, 13, 14, 41, 49, 50, 76, 80, 111, 158, 161, 163, 164, 166, 176, 182

Organoides 142, 143, 146

Osteogênese imperfeita 153

P

PD-1 20, 21, 23, 24, 25, 26, 27, 28, 30, 31, 32, 33

PD-L1 20, 21, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33

Perfil clínico 156, 157, 158, 159, 164

Precursoras neuronais 53

Prevenção 5, 16, 18, 51, 74, 85, 87, 88, 107, 158, 163, 170, 173, 175, 176, 180, 181, 182, 186, 188

Q

Quimioterapia 9, 11, 12, 14, 22, 23, 27, 29, 41, 50, 79, 82, 83, 85, 86, 87, 88, 111, 116, 117, 119, 156, 159, 161, 164, 165, 166, 167, 169, 175, 180

S

Saúde da criança 65

Saúde da mulher 73

Sinais 1, 12, 49, 69, 92, 98, 99, 115, 118, 123, 141, 165

Sintomas 4, 5, 8, 10, 15, 37, 41, 42, 43, 44, 66, 69, 73, 75, 76, 77, 88, 91, 92, 113, 116, 117, 118, 152, 165, 166, 167, 168, 176, 178, 182, 187

T

Tecido adiposo 53, 102, 103

Temefós 94

Terapia celular 132, 133, 135, 139

Tratamento 2, 3, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 23, 27, 28, 30, 36, 37, 38, 39, 41, 42, 43, 44, 48, 49, 51, 53, 65, 66, 67, 68, 71, 73, 74, 76, 77, 79, 80, 81, 82, 83, 85, 86, 87, 88, 91, 92, 113, 116, 117, 118, 119, 124, 133, 139, 140, 145, 156, 158, 160, 161, 164, 165, 166, 167, 169, 175, 176, 179, 180, 182, 186, 187, 188, 189, 190

Tumor cerebral 111

MEDICINA:

Ciências da saúde e pesquisa interdisciplinar



3

-  www.atenaeditora.com.br
-  contato@atenaeditora.com.br
-  [@atenaeditora](https://www.instagram.com/atenaeditora)
-  www.facebook.com/atenaeditora.com.br

MEDICINA:

Ciências da saúde e pesquisa interdisciplinar



3

-  www.atenaeditora.com.br
-  contato@atenaeditora.com.br
-  [@atenaeditora](https://www.instagram.com/atenaeditora)
-  www.facebook.com/atenaeditora.com.br

 **Atena**
Editora

Ano 2021