Data S1.

Search strategy, claim extraction and verification. Data S1 records how the literature underlying the present review was identified and how the claims in Table I and Table SII were extracted; it also states what was not done, so that the methodological reach of the present review is not overestimated.

Literature search. PubMed/MEDLINE (https://pubmed.ncbi.nlm.nih.gov), Web of Science Core Collection (https://www.webofscience.com) and Scopus (https://www.scopus.com) were searched for peer-reviewed English-language articles. The original three-database search covered January 1990 to March 2026 and was performed before manuscript submission. At revision, on September 21, 2026, the update was not applied equally to the three databases, so the coverage period differs by database: PubMed/MEDLINE was updated to September 21, 2026 and the additional records were screened by title and abstract; Scopus was re-searched for the same period but the returned records were not individually screened; Web of Science Core Collection was not re-searched, and its coverage therefore ends in March 2026. The coverage period and the date of execution are reported separately as the date on which a search was run did not necessarily coincide with the end of the publication period it covered.

Emphasis was placed on literature published after January 2020 and on earlier studies that established FABP structure, knockout phenotypes, secretion biology or clinical biomarker associations. Search terms combined 'fatty acid-binding protein' or 'FABP' with individual isoforms (FABP1-FABP9 and FABP12) and with disease or mechanism terms: 'Inflammation', 'tumor microenvironment', 'cancer', 'adipokine', 'PPAR', 'NLRP3', 'MASLD', 'MASH', 'MAFLD', 'NAFLD', 'NASH', 'inflammatory bowel disease', 'colorectal cancer', 'psoriasis', 'skin cancer', 'breast cancer', 'biomarker' and 'therapeutic target'. Reference lists of relevant reviews and mechanistic primary articles were also screened.

Studies were prioritized when they provided genetic or pharmacological perturbation of FABPs *in vivo*; human tissue, circulating biomarker or cohort data; cell-type-specific *in vitro* validation; or integrative reviews clarifying isoform function, ligand routing or therapeutic targeting. Conference abstracts without a full peer-reviewed article, non-English articles without accessible translation and studies without a direct connection to FABP biology were not treated as central.

Registry search. The registry was ClinicalTrials.gov (https://clinicaltrials.gov). In total, two searches were performed at revision on September 21, 2026, covering registry inception to that date; no status, phase or study-type filters were applied to either.

Search 1 was restricted to the intervention field, using: FABP OR 'fatty acid binding protein' OR 'fatty acid-binding protein' OR aP2 OR A-FABP OR E-FABP OR B-FABP OR H-FABP OR L-FABP OR BMS309403 OR SBFI-26 OR HTS01037; it returned 56 records. Search 2 searched the whole record (other terms), using: FABP OR 'fatty acid binding protein' OR 'fatty acid-binding protein'; it returned 395 records.

After removing 54 records common to both searches, 397 unique studies remained. Records were screened against the exported title, conditions, interventions, brief summary and all three outcome-measure fields. In 352 studies, an FABP was a stated outcome measure; 1 record was a false positive arising from an unrelated abbreviation (NCT05897398, in which 'AP2' denotes a French early-access designation); 3 records could not be classified from the exported fields and were retained as unclassified. No study evaluated an agent developed as an FABP-directed therapeutic in any indication; 1 interventional oncology study (NCT05144347) evaluated a compound registered under the sponsor keyword 'Fatty Acid Binding Protein 5'; 2 studies (NCT03799510 and NCT03041766) used a Schistosoma mansoni fatty acid-binding protein as a vaccine antigen. In total, 18 studies were in a cancer population by title or registered condition, but in 16 of these the FABP was measured as an index of gut-barrier or renal injury in a perioperative, nutritional or microbiome context rather than as a cancer-related marker.

Literature search update. The literature search was updated at revision. PubMed/MEDLINE was searched on September 21, 2026 for records published between March 1, 2026 and that date, using the FABP terms alone to avoid inheriting the disease-term list from the original search; 598 records were returned and screened by title and abstract. Scopus was searched with the same terms, limited to publication year 2026, which over-covers the update window; that search returned 832 records, which were not individually screened. Web of Science Core Collection, which was included in the original search, was not searched again.

In total, 4 records were incorporated. These included a report that peritoneal ovarian cancer growth in the omentum proceeds without mature adipocytes, which qualifies the adipocyte-supply model discussed in Section 4; a report of p53-FBXO2-dependent degradation of FABP5 in colorectal cancer, which bears on the contested direction of FABP5 in that tumor type; a multi-omics analysis reporting reduced FABP4 expression in most gynecological tumors; and a 2026 review of FABP-mediated lipid signaling in the tumor immune microenvironment, cited in Section 1. No independent replication of the FABP5-dependent regulatory T-cell phenotype discussed in Sections 3 and 7 was identified.

Claim extraction and verification. During revision, the principal claims of the present review were re-derived from the primary reports rather than from the reviews that cite them. For each claim, the following were recorded in Table SII: The experimental system, species and manipulation; the outcome measured; the direction of the result; the principal limitation; and the primary reference.

Measured outcomes were assigned to one of five classes and were not combined: Inflammatory or immune phenotype; growth or spread of an already established tumor; premalignant change; cancer incidence; and biomarker association in the absence of perturbation.

Extraction was performed by the authors and recorded in full in Table SII so that each statement can be traced to its source. It was a single documented pass; it was not duplicated by independent extractors, and it was not blinded. No summary grade of evidence strength was assigned for the reason given in Section 1.

Primary reports read in full during revision, with the claim each supports: Field CS *et al*., Cell Metab 31: 422-437. e5, 2020-FABP5 and regulatory T-cell suppressive function (Table SII, S-04 and S-05); Ye M *et al*., Int J Biol Sci 19: 3115-3127, 2023-FABP5 and FASN in colorectal cancer (S-01); Seo J *et al*., Cancer Genet 258-259: 151-156, 2021-FABP5 and HIF-1 in colon cancer (S-03); Lu F *et al*., Cancer Sci 114: 3553-3567, 2023-FABP5 and FASN in pancreatic neuroendocrine neoplasia (S-02); Nimptsch K *et al*., BMC Med 21: 391, 2023-circulating FABP4 and colorectal cancer risk (S-06); Adida A and Spener F, Biochim Biophys Acta 1761: 172-181, 2006-FABP4 and PPARγ interaction (S-07); Garin-Shkolnik T *et al*, Diabetes 63: 900-911, 2014-FABP4-dependent PPARγ degradation (S-08); Hohoff C *et al*., Biochemistry 38: 12229-12239, 1999-FABP5 crystal structure and disulfide (S-09); Bennaars-Eiden A *et al*., J Biol Chem 277: 50693-50702, 2002- 4-hydroxynonenal modification of FABP5 (S-13); Zhang Y *et al*., J Invest Dermatol 138: 1925-1934, 2018-epidermal FABP and chemical skin carcinogenesis (S-10).

The two reports underlying the FABP6 claim in Table I, row 11 (Kwon K *et al*., Immune Netw 25: e35, 2025; Ohmachi T *et al*., Clin Cancer Res 12: 5090-5095, 2006) were extracted from the published Results and Methods sections; they are the only claims in Table I for which the primary reports were not obtained in full during revision, and Table SII is annotated accordingly.

What was not done. The present article is a narrative review. No prospective protocol was registered, no PRISMA flow diagram was produced, no formal risk-of-bias instrument was applied and no effect sizes were pooled. Records of the number of items screened and excluded during the original literature search were not kept. These counts have not been reconstructed after the fact, as a count produced retrospectively would not represent the screening process it purports to describe. No summary grading of evidence strength was applied. A single label, such as ‘strong’, would have to be earned by studies that agree on the disease, the cell type and the outcome measured, and for most FABP circuits, the available human association data, animal perturbation experiments and cell-based mechanistic work do not agree on all three. The classification that is retained in Section 6 concerns the development status of an intervention, which is a matter of record rather than a judgment about the underlying biology.

Figure S1. Structural and evolutionary features of the mammalian FABP family. (A) Conserved β-barrel fold, shown for mouse FABP4 in complex with linoleic acid (PDB 2Q9S): 10 antiparallel β-strands (blue) and two capping α-helices (orange) enclose a water-filled internal cavity, and the ligand is proposed to enter through the portal region formed by helix αII and the βC-βD and βE-βF turns (1,2,20-23). (B) Simplified phylogeny of the 10 mammalian isoforms, grouped by intracellular lipid-binding protein subfamily; subfamily I, which comprises the cellular retinoid-binding proteins rather than FABPs, is not shown (1,28,29). (C) Chromosomal distribution (human, GRCh38). FABP4, FABP5, FABP8, FABP9 and FABP12 lie within a single tandem-duplication cluster at 8q21.13; FABP7 is phylogenetically related to this group but maps to a separate locus at 6q22.31 (1,27). Tissue distribution and ligand preferences are given in Table SI. Chr, chromosome; FABP, fatty acid-binding protein; GRCh38, Genome Reference Consortium human build 38; iLBP, intracellular lipid-binding protein; PDB, Protein Data Bank; PMP2, peripheral myelin protein 2.

